Comments received on draft IACG recommendations 29 January – 19 February 2019

Member States

- Australia
- Austria
- Brazil
- Canada
- Chile
- Colombia
- European Commission
- Finland
- France
- Gabon
- Germany
- Japan
- Luxembourg

CSOs/NGOs

- Antibiotic Resistance Coalition (ARC)
- Association for Professionals in Infection Control and Epidemiology (APIC)
- British Society for Antimicrobial Chemotherapy (BSAC)
- Center for Genetic Engineering and Biotechnology of Cuba
- Centre for Science and Environment (CSE)
- Consumer Reports
- European & Developing Countries Clinical Trials Partnership (EDCTP)
- European Association of Hospital Pharmacists (EAHP)
- Jean Carlet, President, World Alliance Against Antibiotic Resistance

- Mali
- Mexico
- Netherlands
- New Zealand
- Norway
- Peru
- Singapore
- Spain
- Sweden
- Switzerland
- United Kingdom
- United States
- Keep Antibiotics Working (KAW)
- Korean Society for Antimicrobial Therapy
- MSF Access Campaign
- Natural Resources Defense Council (NDRC)
- ReAct
- RESULTS UK
- Swedish Water House (SIWI)
- The International Union Against Tuberculosis and Lung Disease (The Union)
- Universities Allied for Essential Medicines -Europe
- US Pharmacopeia
- WaterAid
- World Veterinary Association (WVA)

Private Sector

- AMR Industry Alliance
- Aviva
- Centrient Pharmaceuticals
- FAIRR
- HealthforAnimals
- International Meat Secretariat

- International Poultry Council (IPC)
- International Union of Food, Agricultural, Hotel, Restaurant, Catering, Tobacco and Allied Workers' Associations (IUF)
- RPS Diagnostics

Individual

- Annamari Heikinheimo, Dept. of Food Hygiene and Environmental Health, Faculty of Veterinary Medicine, University of Helsinki
- Babacar Ndoye, AMR/IPC Expert- consultant
- Daniel Carucci, Global Medical Director, McCann Health
- Heidi Vesterinen, Researcher, One Health Workforce, University of Minnesota
- Les Sims, Director, Asia Pacific Veterinary Information Services
- Marc Mendelson, Professor of Infectious Diseases, University of Cape Town
- Mark D. Sobsey, Research Professor,
 University of North Carolina, Gillings School of
 Global Public Health
- Other
 - Gavi, the Vaccine Alliance
 - Global Antibiotic Research and Development Partnership (GARDP)
 - Global Antimicrobial Resistance (AMR)
 Research and Development (R&D) Hub
 - Joint Programming Initiative on Antimicrobial Resistance (JPIAMR)
 - Medicines for Malaria Venture
 - Medicines Patent Pool (MPP)
 - Pew Charitable Trusts
 - South Centre
 - Stop TB Partnership
 - United Nations Development Programme (UNDP)
 - Wellcome Trust
 - World Farmers Organisation

- Michael Ryan, OECD
- Mohammed Ishaaq Datay et al.
- Nobuko Ichikawa & Matthias Long, ERDB
- Peter Collignon, Infectious Diseases Physician and Microbiologist, Canberra Hospital
- Prateek Sharma, MSc Student, School of Population and Public Health, University of British Columbia
- Sabiha Essack, South African Research Chair in Antibiotic Resistance and One Health Antimicrobial Research Unit, University of KwaZulu-Natal
- Wendy Thompson, Doctoral Research Fellow, University of Leeds

DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE

Comments from Australia 19 February 2019

Australia commends the Ad Hoc Interagency Coordination Group on Antimicrobial Resistance for its draft recommendations, and welcomes the opportunity to comment.

We welcome the strong emphasis on the importance of a comprehensive One Health approach to addressing AMR – facilitating the coordinated, collective efforts of the human, terrestrial and aquatic animal and plant health, agricultural and environmental sectors. Australia strongly supports a One Health approach to collaboration, noting the need for complementarity between current initiatives to ensure a unified approach. We recognise the need to maintain urgency and political momentum, and appreciate the IACG's focus on a coordinated and concerted effort to enhance current actions and reduce duplication.

Australia strongly supports the recommendations in Section A to accelerate progress in countries, particularly in implementation of One Health National AMR Action Plans. The inclusion of specific timeframes in this section would strengthen the justification for urgent action.

Australia supports, in principle, the recommendations in Section B, but queries whether these have been tested with the relevant stakeholders, noting that an acknowledgment of their general support would add weight to the final report.

Australia appreciates the recommendations in Section C, providing concrete actions to optimise the contributions of civil society and the private sector to the AMR response. We consider this clear definition a positive contribution to the global dialogue.

Australia also welcomes the recommendations in Sections D and E towards AMR 'mainstreaming'. We note the recognition of UN reform as an opportunity to strengthen joint One Health action on AMR, and support the recommendation to integrate AMR activities into UN Development Assistance Frameworks, based on country priorities and needs.

Australia commends the efforts of the Tripartite Plus, and acknowledges the recommendations in Section E for continued and increased support to the Tripartite Plus, as well as enhanced harmonisation in the coordination of activities. Noting the existing roles of technical agencies, the importance of avoiding duplication in collaborative global action on AMR, and the value of building on established structures to ensure simplicity and sustainability, we would welcome further rationale for the proposals on new global governance mechanisms.

In finalising its report, we would encourage the IACG to further elaborate on recommendations E1 and E2; including:

- the specific value-add of the proposed new mechanisms, noting that a number of the functions outlined are already being performed by technical agencies;
- expected resourcing implications of the proposed new mechanisms;
- advantages and disadvantages of new organisational structures versus strengthening the Tripartite Plus, potentially with a dedicated Secretariat and budget; and
- relationship of the proposed new mechanisms with the Tripartite Plus, particularly at the level of the Secretariat (e.g. how would the proposed new Secretariat relate to existing Secretariat structures?)

Australia considers that any new mechanism would need a clear comparative advantage, recognising that it would take time for a new mechanism to be fully established, and that broad political support would be necessary for it to have the influence and resources to deliver effectively. If new mechanisms are needed, consideration should be given to time-bound mandates with clear procedures for formal review.

In finalising its report, Australia also suggests the IACG consider:

- providing further analysis of the amount of time there is to act in order to make real gains in addressing/halting AMR;
- indicating prioritisation of recommendations, and where possible timeframes to support urgency for action; and
- reflecting that overuse and misuse of antimicrobials also occurs in human health, not solely in animal health (page 2, paragraph 2).

IACG Draft Recommendations on Antimicrobial Resistance

(For public discussion prior to finalization; January 2019)

Comments by Austria

In principle, Austria supports the recommendations proposed by the IACG. Having said this, Austria, proposes, in addition, the following amendments:

(1) To page 4, Recommendation A 1, considerations on the recommendation:

"The IACG recognizes that in settings where trained <u>physicians</u> are in short supply, non-physicians (such as nurses, paramedics and community health workers) and veterinary paraprofessionals <u>should</u> also_be trained and authorized_to prescribe or administer antimicrobial agents."

With regard to the training of" veterinary paraprofessionals ", it would be useful to define minimum standards and criteria for obtaining an authorization, in particular with respect to the training concerning the prescription or administration of antimicrobials.

(2) To page 5, Recommendation A 2:

The considerations for this recommendation recognize the major differences in Member States' health systems and the different needs. Therefore, <u>Austria deems it necessary that the design of the national action plans should be as flexible as possible.</u>

Hence, it would be useful to **include this flexibility** not only in the considerations for this recommendation, but **also directly in Recommendation A 2 itself**.

(3) To pages 14 to 18, E. Strengthen Accountability and Global Governance:

Establishing a "One Health Global Leadership Group for Antimicrobial Resistance" could help avoid duplication of efforts within the organizations concerned across the UN system.

Austria therefore explicitly supports this recommendation.

(end of text)

Brazil

From: <u>Matheus Machado de Carvalho</u>

To: <u>IACG-secretariat</u>

Cc: <u>Durval Luiz de Oliveira Pereira</u>

Subject: Draft recommendations of the IACG-AMR: Feedback from the Brazilian government (Ministry of Agriculture,

Livestock and Supply of Brazil)

Date: Tuesday, February 19, 2019 22:08:59

Attachments:

Dear colleagues,

Regarding the Draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance, I convey, therefore attached, comments of the Brazilian government, more especifically from the Ministry of Agriculture, Livestock and Supply (MAPA) of Brazil (in portuguese).

Due to the renewal of the Brazilian government, we were not able to convey also the final comments of the Ministry of Health up to February 19th.

I take the opportunity to highlight a free translation of the conclusion of the attached document:

"MAPA's technical area therefore reiterates its doubts as to the need for and effectiveness of the creation of a new governance structure to address the issue, since it is already addressed by multilateral organizations such as WHO, FAO and OIE, which have recently strengthened commitment to working together on a Memorandum of Understanding. The document does not clarify how the composition, governance and functioning of these groups will be determined, which is a factor of additional concern about its creation."

Regards,

Matheus Carvalho Primeiro Secretário/First Secretary Ministério das Relações Exteriores/Ministry of Foreign Affairs of Brazil

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Esta mensagem foi verificada pelas ferramentas de detecção de ataques do Ministério e nenhuma ameaça cibernética foi encontrada. Não obstante, recomenda-se cautela, especialmente se solicitar dados pessoais e senhas ou se contiver anexos.

Brazil

From: Regiane Tigulini de Souza Jordão

To: <u>IACG-secretariat</u>
Cc: <u>André Luiz de Abreu</u>

Subject: BRAZIL_Public discussion_DRAFT RECOMMENDATIONS IACG on AMR

Date: Wednesday, February 20, 2019 02:57:36

Dear all,

In response to the draft recommendations of the Interagency Coordination Group on Antimicrobial Resistance, we have compiled the considerations of the Ministries of Health and Agriculture, Livestock and Supply as follows.

Após a análise do documento em consulta pública "Rascunho das Recomendações do Grupo ad hoc de Coordenação Interagências sobre Resistência aos Antimicrobianos - IACG", reiteramos preocupação já expressa no Memorando 108 para outro documento elaborado pelo IACG, "Future Global Governance for Antimicrobial Resistance".

O atual documento recomenda no item E o estabelecimento de um "Grupo de Liderança Global *One Health* em Resistência aos Antimicrobianos" (recomendação E1), apoiado por um Secretariado, para manter o apoio político e visibilidade, advogar por ações, monitorar e relatar progressos, aumentar envolvimento multisetorial, prover aconselhamento, monitorar financiamentos, identificar prioridades de pesquisa e desenvolvimento, bem como definir necessidades de financiamentos em relação à resistência aos antimicrobianos.

O IACG propõe que esse Grupo de Liderança seja composto por um pequeno grupo de atuais ou ex Chefes de Estado, Ministros de Agricultura, Saúde e Meio Ambiente, Diretores das agências Tripartite, da ONU e outras agências internacionais, Diretores de Bancos regionais, além de líderes globais representando a saúde humana, animal e sanidade vegetal, produção de alimentos e meio ambiente.

Adicionalmente, recomenda a criação de um "Painel Independente em Evidências para Ação contra a Resistência aos Antimicrobianos" para monitorar os Estados Membros e prover relatórios regulares sobre a ciência e evidências relacionadas com a resistência aos antimicrobianos e recomendações de opções para adoção e mitigação. Deve incluir especialistas dos setores de saúde humana, animal (terrestre e aquático), sanidade vegetal, bem como do meio ambiente, produção e inocuidade de alimentos.

Reiteramos, portanto, nossa dúvida sobre a necessidade e efetividade da criação de nova estrutura de governança para tratar do tema, uma vez que o mesmo já é tratado por organismos multilaterais como a OMS, FAO e OIE, que reforçaram recentemente o seu compromisso de trabalho conjunto em um Memorando de entendimento. O documento não esclarece como será determinada a composição, governança e funcionamento desses grupos, sendo esse um fator de preocupação adicional quanto à sua criação.

Em relação à Recomendação D2 que enfatiza a necessidade de aumentar o investimento na resposta global à resistência antimicrobiana, consideramos como de fundamental importância dispor de mecanismos de investimentos, no entanto, destacamos o cuidado necessário ao tecer recomendações respeitando as diferentes realidades sociais, econômicas, culturais e epidemiológicas. Analisar e estabelecer o investimento mínimo necessário para o desenvolvimento das atividades referentes à AMR é fundamental, mas também é preciso atribuir eficiência aos recursos públicos existentes. Considerando, inclusive, as recomendações dos órgãos de controle governamental, para cada realidade faz-

se necessário avaliar e selecionar a opção de melhor custo-efetividade que, por vezes, não aborda exclusivamente questões de AMR mas que seja capaz de gerar o impacto esperado e, ao mesmo tempo, otimize os investimentos públicos. Além disso, a contribuição global pode se dar de diferentes maneiras, além do investimento financeiro: cooperações técnicas de intercâmbio para formação ou capacitação de recursos humanos, o estabelecimento de relação mútua de compartilhamento de evidências científicas sobre o assunto e estímulo para que os países produzam tais evidências, encontros periódicos para discussão e troca de experiências entre os países sobre a implantação dos seus Planos de Ação Nacional, webinar ou webconferência. A inexistência de um planejamento mínimo anterior pautado em informações concretas, inviabiliza pleitear o recurso necessário e adequadamente dimensionado aos governos.

Colocamos nosso corpo técnico à disposição para contribuições que se fizerem necessárias, por meio dos endereços de email:

Atenciosamente.

André Luiz de Abreu, Department of Surveillance of Communicable Diseases - Deputy Director, Ministry of Health of Brazil.

Esta mensagem pode conter informação confidencial e/ou privilegiada. Se você não for o destinatário ou a pessoa autorizada a receber esta mensagem, não pode usar, copiar ou divulgar as informações nela contidas ou tomar qualquer ação baseada nessas informações. Se você recebeu esta mensagem por engano, por favor avise imediatamente o remetente, respondendo o e-mail e em seguida apague-o.

Brazil - unofficial translation

After reviewing the public consultation document "Draft Recommendations of the Ad Hoc Interagency Coordination Group on Antimicrobial Resistance - IACG", we reiterate concern already expressed in Memorandum 108 to another IACG document, "Future Global Governance for Antimicrobial Resistance".

The current document recommends in item E the establishment of a "One Health Global Leadership Group on Antimicrobial Resistance" (E1 recommendation), supported by a Secretariat, to maintain political support and visibility, advocate for action, monitor and report on progress, increase multisectoral involvement, provide counseling, monitor funding, identify research and development priorities, and define funding needs for antimicrobial resistance.

The IACG proposes that this Leadership Group be composed of a small group of current or former Heads of State, Ministers of Agriculture, Health and Environment, Directors of Tripartite Agencies, UN and other international agencies, Directors of Regional Banks, and global leaders representing human, animal and plant health, food production and the environment.

In addition, it recommends the creation of an "Evidence Independent Panel for Action against Antimicrobial Resistance" to monitor Member States and provide regular reports on antimicrobial resistance science and evidence and recommendations for options for adoption and mitigation. It should include specialists from the human, animal (terrestrial and aquatic), plant health, environment, food and food safety sectors.

We therefore reiterate our doubts about the need for and effectiveness of the creation of a new governance structure to deal with this issue, since it is already addressed by multilateral organizations such as WHO, FAO and OIE, which have recently strengthened their commitment to work set out in a Memorandum of Understanding. The document does not clarify how the composition, governance and functioning of these groups will be determined, which is a factor of additional concern about its creation.

Regarding Recommendation D2, which emphasizes the need to increase investment in the global response to antimicrobial resistance, we consider that it is fundamentally important to have investment mechanisms, however, we emphasize the care needed to make recommendations respecting different social, economic, cultural, and epidemiological studies. Analyzing and establishing the minimum investment needed for the development of AMR activities is essential, but it is also necessary to efficiently use existing public resources. Considering, also, the recommendations of the government control organs, for each reality makes it necessary to evaluate and select the most cost-effective option, which sometimes does not exclusively address AMR issues but is capable of generating the expected impact while optimizing public investments. In addition, the overall contribution can be made in a number of ways, in addition to financial investment: technical exchanges for training or training of human resources, establishing a mutual relationship of sharing scientific evidence on the subject and stimulating countries to produce such evidence, periodic meetings for discussion and exchange of experiences among countries on the implementation of their National Action Plans, webinar or web conferencing. The lack of a previous minimum planning based on concrete information, makes it impossible to advocate for the necessary and appropriately sized resource to the governments.

From: <u>Matheus Machado de Carvalho</u>

To: <u>IACG-secretariat</u>

Cc: <u>Durval Luiz de Oliveira Pereira</u>

Subject: Draft recommendations of the IACG-AMR: Feedback from the Brazilian government (Ministry of Agriculture,

Livestock and Supply of Brazil)

Date: Tuesday, February 19, 2019 22:08:59

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Regards,

Matheus Carvalho Primeiro Secretário/First Secretary Ministério das Relações Exteriores/Ministry of Foreign Affairs of Brazil

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MINISTÉRIO DA AGRICULTURA, PECUÁRIA E ABASTECIMENTO Secretaria de Comércio e Relações Internacionais Departamento de Temas Técnicos, Sanitários e Fitossanitários Esplanada dos Ministérios, Bloco D, Sala 340, Brasília/DF, CEP: 70043900 - http://www.agricultura.gov.br

21000.005399/2019-11

Oficio Nº 588/2019/CGSF/DTSF/SCRI/MAPA - MAPA

Brasília, 18 de fevereiro de 2019.

Ao Senhor Durval Luiz de Oliveira Pereira Chefe interino da Divisão de Temas Sociais Ministério das Relações Exteriores Esplanada dos Ministérios - Bloco H 70170-900 - Brasília – DF

Assunto: Urgente. Nações Unidas. Temas sociais. Saúde. Grupo Ad hoc de Coordenação Interagênicas (IACG) sobre resistência antimicrobiana. Comentários do MAPA.

Senhor Chefe,

Em referência à MO Nº 208 de 30/01/19, a área técnica do Ministério da Agricultura, Pecuária e Abastecimento - MAPA faz os seguintes comentários:

Após análise da referida documentação, reitera-se preocupação já expressa no Memorando 108 para outro documento elaborado pelo IACG, "Future Global Governance for Antimicrobial Resistance" enviado por meio do Ofício nº 2485/2018/CGSF - MAPA, de 24/08/18.

O atual documento recomenda no item E o estabelecimento de um "Grupo de Liderança Global One *Health* em Resistência aos Antimicrobianos" (recomendação E1), apoiado por um Secretariado, para manter o apoio político e visibilidade, advogar por ações, monitorar e relatar progressos, aumentar envolvimento multisetorial, prover aconselhamento, financiamentos, identificar prioridades de pesquisa e desenvolvimento, bem como definir necessidades de financiamentos em relação à resistência aos antimicrobianos.

O IACG propõe que esse Grupo de Liderança seja composto por um pequeno grupo de atuais ou ex Chefes de Estado, Ministros de Agricultura, Saúde e Meio

Ambiente, Diretores das agências Tripartite, da ONU e outras agências internacionais, Diretores de Bancos regionais, além de líderes globais representando a saúde humana, animal e sanidade vegetal, produção de alimentos e meio ambiente.

Adicionalmente, recomenda a criação de um "Painel Independente em Evidências para Ação contra a Resistência aos Antimicrobianos" para monitorar os Estados Membros e prover relatórios regulares sobre a ciência e evidências relacionadas com a resistência aos antimicrobianos e recomendações de opções para adoção e mitigação. Deve incluir especialistas dos setores de saúde humana, animal (terrestre e aquático), sanidade vegetal, bem como do meio ambiente, produção e inocuidade de alimentos.

A área técnica do MAPA reitera, portanto, a dúvida sobre a necessidade e efetividade da criação de nova estrutura de governança para tratar do tema, uma vez que o mesmo já é tratado por organismos multilaterais como a OMS, FAO e OIE, que reforçaram recentemente o seu compromisso de trabalho conjunto em um Memorando de entendimento. O documento não esclarece como será determinada a composição, governança e funcionamento desses grupos, sendo esse um fator de preocupação adicional quanto à sua criação.

Combined input from the Government of Canada on the Draft IACG Recommendations

General Comments & Suggestions:

- We are pleased to see that the IACG recommendations consistently take a One Health approach to addressing AMR, and we are pleased to see that the importance of giving "due consideration to country-specific contexts, capacity and infrastructure" was noted. We feel that this is a critical element to keep in mind.
- The recommendations are in-line with ongoing discussions we have seen, however we note that the extent to which many countries, including Canada, will be able to take action will depend on domestic context, need and priorities.
- We note with interest the ongoing discussions around governance and monitoring, but feel it would be helpful to clarify within the recommendations how these two bodies (the Leadership Group and the Independent Panel) will be established and financed, how they will align with, and avoid duplication of, ongoing efforts in these areas (e.g. R&D priority setting, the costs of AMR, etc.) and accountability.
- We noted "mainstreaming of efforts to combat antimicrobial resistance" in the guiding principles.
 We think it is an important concept, and suggest including in the recommendations or considerations, ideas and approaches for achieving this.

Wording/technical

- For clarity purposes, we suggest using the term "antimicrobial" throughout the document in place of the term "antibiotic". Antibiotic as a term is restrictive in its application. It can either refer only to those agents active against bacteria, to the exclusion of fungi, protozoa et al., or it can be interpreted as only referring to those antimicrobial agents produced naturally by bacteria/molds, to the exclusion of chemically synthesized agents. Using the term "antimicrobial" consistently will prevent any such ambiguity.
- We note that throughout the document, there is often mention of 'prudent use'. We suggest that whenever the term 'prudent use' is included, there be additional language stating there should be efforts made to reduce the need for use, such as through IPC, husbandry, and other preventive measures. We feel this additional language best reflects efforts to address AMR.

Specific Feedback:

<u>Recommendation A1:</u> The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health.

This recommendation must be supported by efforts both to reduce the need for antimicrobials and improve access through:

a. Lowering the prevalence of infection through clean water, sanitation and hygiene;

- b. Decreasing the likelihood of diseases and their spread through delivery of existing vaccines and strengthening infection prevention and control measures;
- c. Ensuring best practices in terrestrial and aquatic animal and plant health, food production and waste management;
- d. Supporting behaviour change through effective communication and incentives targeted at the public and professionals in human, terrestrial and aquatic animal and plant health, as well as food production and the environment;
- e. Developing national instruments based on international standards for equitable access to and prudent use of existing and new quality-assured antimicrobials in humans, animals, plants and food production, as well as waste and water management in health care, manufacturing and farming-related activities; and
- f. Strengthening national surveillance, regulatory and accountability mechanisms.
- Overall these recommendations are in alignment with discussions at the G7/G20.
- We notice that certain elements of this recommendation related to access and equity seem to be duplicated in recommendation B2.
- Item F appears to be very broad in scope, and does not take into account countries that already have strong systems in place. We recommend the following alternative wording to improve clarity: "Maintain, and where necessary strengthen, national surveillance, regulatory and accountability mechanisms." We also notice that Item F appears to be duplicated in recommendation A2, Item B.
- Suggest clarifying the meaning of "stockouts", which appears in the text under this recommendation.

<u>Recommendation A2:</u> The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs that, at a minimum, include:

- a. Prioritized actions and interventions that are specific to the national context and that are costed and funded, including with adequate domestic resource allocations;
- b. Strengthening key national systems for infection prevention, monitoring, integrated surveillance, procurement of health commodities and waste management;
- c. Technical co-operation, capacity development, research and advocacy components, including support for champions at national and local levels to mobilize action on antimicrobial resistance; and
- d. Effective national coordination, accountability and governance mechanisms.
- We suggest updating the text in item "A" to read "Prioritized actions and interventions that are specific to the national context, capacity and infrastructure, and that are costed and funded, including with adequate domestic resource allocations", to align with the language in the guiding principles.
- Recommend clarifying the meaning of "procurement of health commodities".

Recommendation A3: The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins).

 For accuracy, we recommend the following alternative wording: "Highest Priority Critically Important <u>Antimicrobial</u> Agents", rather than "<u>Antibiotic</u> Agents", in line with our first wording/technical comment. <u>Recommendation B1:</u> The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials - particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials - for human, terrestrial and aquatic animal and plant health through:

- a. Financial and non-financial incentives strategically targeting the most important research and development needs, scientific challenges, and market barriers based on the principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance; and b. Building upon existing Product Development Partnerships in human health and establishing more of them, particularly for terrestrial and aquatic animal and plant health.
- We are supportive of this recommendation, and in particular, we support the inclusion of, and importance to maintain, non-financial incentives with respect to regulatory contribution to therapeutic product innovation and development.
- We emphasize the importance of Member States' ensuring that work builds on product development partnerships and funding initiatives such as those developed by the Global Antibiotic Research and Development Partnership (GARDP), UNITAID, the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR), the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), Innovative Medicines Initiative (IMI) and TB-Alliance.

<u>Recommendation B2:</u> The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

- While we are supportive of this recommendation, we notice some duplication/ repetitiveness with many of the items listed under recommendation A1.
- Preserving the effectiveness of existing therapeutic options is important to efforts to combat AMR.

<u>Recommendation B3:</u> The IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context by:

- a. Undertaking coordinated global mapping of research and development activities and funding to address antimicrobial resistance;
- b. Establishing and maintaining a platform for sharing information on research and compounds in development in both ongoing and completed research and development activities;
- c. Promoting synergies and opportunities for collaboration among funders and researchers in human, animal and plant health, and the environment; and
- d. Promoting openness and transparency in data from all research and monitoring and surveillance sources.
- We note that Item B could be enhanced to improve clarity. Also, as it is currently written, it seems to only address the development of new antimicrobial compounds, while it could be broadened to include other products (e.g. therapeutics, diagnostics, and vaccines) as well.
- It is important to note that in addition to product development, research in other areas remains critical to support efforts to combat AMR, including (but not limited to) mechanisms of resistance development, transmission, incidence and usage patterns.
- We note that work in this area should build on existing efforts, and not duplicate the work of, networks and initiatives in this area, such as those undertaken by Tripartite agencies, the Global AMR R&D Hub, GARDP, CARB-X and JPIAMR.

<u>Recommendation C1:</u> The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels through:

- a. Strengthening their roles in accountability, advocacy, monitoring progress and ensuring prudent use of antimicrobials;
- b. Promoting synergies with consumer and civil society groups active in other sectors, including in climate change and the environment, responses to HIV, TB and malaria, Universal Health Coverage and other aspects of the SDGs; and
- c. Provision of political, financial and technical support for civil society organizations to enhance their engagement, including for work with governments.
- Suggest adding to the recommendation items: sharing of lessons learned, best practices, or successes related to civil society engagement, particularly those that have resulted in changes in practice.

<u>Recommendation C2:</u> The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels in order to ensure:

- a. Affordable access, prudent use and stewardship of antimicrobials;
- b. Ethical production, distribution and marketing practices, including through environmentally sustainable production and waste management and the elimination of inappropriate incentives to sell antimicrobials;
- c. Engagement by the private sector in collaborative efforts to collect, analyze and use data and realign economic incentives to improve production, distribution and marketing practices; and
- d. Contributions to addressing antimicrobial resistance through testing of innovative approaches, corporate social responsibility, and similar initiatives.
- Suggest noting in the considerations for this recommendation the pledges that industries made under the 2016 Industry Declaration on AMR.
- We recommend clarifying what is meant by "corporate social responsibility".
- Suggest considering including language addressing the development of new, safe, effective and affordable drugs in this section.

<u>Recommendation D1:</u> The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and One Health "lens" when making investments through:

- a. Official Development Assistance;
- b. South-South cooperation;
- c. The International Development Association (IDA) replenishment process from IDA19 onwards;
- d. Financial support, grants, loans, credits and insurance for terrestrial and aquatic animals and plants, health, development, food systems, manufacturing of health products, the environment and other relevant areas.
- No comments

Recommendation D2: The IACG emphasizes the need for increased investment in the global response to antimicrobial resistance. It urges existing and future financing mechanisms in human, animal and plant health, as well as food production and the environment - including Gavi – the Vaccine Alliance, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Global Financing Facility, Multilateral Climate Funds, Unitaid, as well as future financing streams for Universal Health Coverage and other priority development issues, and their donors - to give antimicrobial resistance greater

priority in their resource allocations. It further calls upon public, private and philanthropic donors in human, animal and plant health, as well as food production and the environment, to increase funding to contribute to addressing antimicrobial resistance, including to support implementation of National Antimicrobial Resistance Action Plans.

No comments

<u>Recommendation E1:</u> The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat, to:

- a. Maintain urgency, public support, political momentum and visibility of the antimicrobial resistance challenge on the global agenda, and set targets;
- b. Advocate for action, including support for the expanding work of the Tripartite agencies (FAO, OIE and WHO), UN Environment (UNEP) and other international and regional entities;
- c. Monitor and report on progress, gaps and accountability in the global response to antimicrobial resistance;
- d. Expand multi-stakeholder engagement by establishing a partnership platform with the participation of Member States, UN agencies, international and intergovernmental organisations and regional entities, civil society, the private sector, researchers and other key stakeholders to develop and work towards a shared global vision and coordinated action on antimicrobial resistance;
- e. Provide advice and guidance on reports of the Independent Panel on Evidence for Action against Antimicrobial Resistance (recommendation E2);
- f. Monitor and advocate for the inclusion of antimicrobial resistance and a One Health "lens" in investments and programmes of major financing instruments for agriculture, health, development, food production and other relevant areas (recommendation D1);
- g. Identify priorities for research and development and facilitate implementation research in a One Health context; and
- h. Define the financial needs and gaps for the global response to antimicrobial resistance, including the costs of inaction and anticipated returns on investment.
- While we recognize the role that a Leadership Group on AMR could play in maintaining momentum
 in global efforts to combat AMR, we note the importance of avoiding duplication with existing
 bodies working in this area and ensuring alignment with ongoing efforts.
- If such a group were to be established, many factors would need to be considered in consultation with Member States, including:
 - o The source of funding for the Leadership Group on AMR.
 - Accountability (who the Leadership Group would report to).
 - The relationship with, and expectations of, Member States, Tripartite agencies, civil society and industry.
- Related to item "A", we note that target setting is best done at the national level, as recognized in the recent draft of the Global Framework for Development and Stewardship to Combat AMR.

Recommendation E2: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.

• While we support this recommendation, we note the importance of avoiding duplication in this area and ensuring alignment with ongoing efforts.

- We note that consensus on approaches to addressing AMR and its associated threats, as mentioned
 in the first consideration, may depend heavily on country-specific context, and suggest that
 language around this be added.
- Suggest that the relationship (if any) between this recommendation and E1 be clarified.
- Given the limited resources available to address AMR, it is important to consider the cost of establishing two new groups/bodies as outlined in recommendations E1 and E2.

<u>Recommendation E3:</u> The IACG requests the Tripartite agencies (FAO, OIE and WHO) together with UNEP and other UN agencies, in the context of UN reform, to further strengthen joint One Health action, based on country priorities and needs, by enhancing their organizational capacity and providing adequate and sustainable core funding for antimicrobial resistance-related activities in order to:

- a. Integrate antimicrobial resistance-related activities into country UN Development Assistance Frameworks;
- b. Provide and update effective normative guidance, standards and tools when needed;
- c. Advise on priority evidence-based interventions and actions;
- d. Provide coordinated technical co-operation and capacity building, including One Health regional platforms for technical co-operation; and
- e. Guide, support, monitor and evaluate implementation, including on infection prevention, integrated surveillance, data quality and harmonization, risk assessment, and demand forecasting and supply management.
- We support this recommendation, and we support the reference to a "Joint Periodic Review", as mentioned in the text accompanying this recommendation.
- Suggest including a clarification the meaning of "normative guidance".
- Recommend outlining how the monitoring and evaluation activities outlined in item "E" align with those currently underway.

<u>Recommendation E4:</u> The IACG recognizes the ongoing process led by Member States to develop the <u>Global Development and Stewardship Framework to Combat Antimicrobial Resistance</u> and urges the Tripartite agencies (FAO, OIE and WHO) and UNEP to expedite its development in line with the scope described in the 2015 World Health Assembly resolution on antimicrobial resistance (WHA68.7). As Member States finalize this process, they should also consider the need for new international instruments.

While the issue of international instruments has been raised previously, including during discussions
around the Global Framework for Development and Stewardship to Combat AMR, there has not
been sufficient discussion to date, or information included in this report, to determine with
confidence what such instruments could do, the appropriate mechanisms, or the implications.

Chile

Comments to the public discussion of the "Draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance"

Member State: Chile

Revision and comments made by:

- 1. Dr. Juan Carlos Hormazabal, Chief of Infectious Disease Department, Public Health Institute, Ministry of Health.
- 2. Dr. Jorge Valdebenito, National Antimicrobial Resistance Action Plan Secretariat, Division of Disease Prevention and Control, Undersecretariat of Public Health, Ministry of Health.
- 3. Constanza Vergara M.V., Adviser, Chilean Food Safety and Quality Agency, Ministry of Agriculture.

^{*}Comments are in bold to mark insertion and strike down for deletion.

Recommendation	Comment	Rationale
A1, letter B.	Decreasing the likelihood of diseases and their spread through delivery of existing vaccines and strengthening infection prevention and control measures national policies	This should be part of national policies that allow secure governmental resources.
A1, letter D	Add text that encourage the best practices among the community and focus on limitation pharmaceutical industry marketing of antimicrobials, sale under prescription and treatment follow, as a part of the behavior change.	
A1,	Add an action at the end: "To promote integrated antimicrobial resistance surveillance through the formal collaboration between Ministries of Health, Agriculture, Economy and other related government partners"	To take actions that ensure the best practices in the antimicrobial use
Considerations for recommendation A1, second bullet, first sub bullet "Addressing shortages and stockouts"	Add a consideration for antimicrobial drugs that are take out from the market by pharmaceutical industry, but their use in combination with other antimicrobial agent could be still efficient.	

Considerations for recommendation A1, second bullet, second sub bullet "Effective national-level antibiotic demand forecasts"	Add into the consideration, countries that doesn't have antimicrobials manufacturers and shortage not always are cause by under development of a forecast demand model.	
Considerations for recommendation A1, second bullet,	Add a new bullet Support elaboration of National Critically important list of Antibiotics,	Each country should elaborate their own list based on their animal and human epidemiology that ensuring equitable and affordable access to and stewardship. International Organizations could also support capacity building that allow countries to elaborate their own antibiotic critical important list.
Considerations for recommendation A1, second bullet, sub bullet "Tackling substandard and falsified medical products"	At the end of the paragraph add; The implementation of National antimicrobial regulatory agencies should be promoted	Universal health coverage by their own is not enough to tackle antibiotic counterfeit Also National Antimicrobial Regulatory Agencies could help to create policies to assure the quality of the available antibiotics.
Considerations for recommendation A1, third bullet	The IACG recognizes that in settings where trained prescribers are in short supply, non-physicians (such as nurses, paramedics and community health workers) and veterinary paraprofessionals may also be trained and authorized to prescribe or administer some antimicrobial agents	We do not agree with this consideration since due the complexity of AMR and pharmacodynamics, the antibiotic prescription should be done by health professional who received formal education on these aspects. Training is considered in many countries as an informal way of preparation. Efforts should be focus on include AMR and pharmacology in more non-physician or veterinarian health professionals educational curriculum.

Canaidanation		There isn't any avidence that
Consideration for Recommendation A2, last bullet.	The IACG emphasizes that One Health integrated surveillance and monitoring systems need to be established, coordinated and integrated, covering human, terrestrial and aquatic animal and plant health, food production and the immediate food production environment environment.	There isn't any evidence that support that plant pathogens could develop foodborne AMR, plant should be only part of the surveillance when they are part of the food production chain. Plant health is a broad term that could lead to confusion on the surveillance of non-edible ones. The same rationale applies to the environment term. Surveillance programs represent a huge economic burden to countries, so, should be targeted to protect public health monitoring places where foodborne AMR can occur.
	To the extent possible, they should also provide harmonized or equivalent data that can be easily compared, exchanged, used and aggregated locally, nationally and globally and ensure this data will not be used as a trade barrier	Understanding that collaboration among countries and the exchange of AMR surveillance information could be useful, the data could be easily use as a trade barrier when categorization of countries due their AMR status applies, specially for foodborne pathogens and food trade.
Recommendation for consideration A3, third bullet	After this sentence add text in bold; as described in the OIE Terrestrial Animal and Aquatic Animal Health Codes or the Codex Alimentarius Standard "GUIDELINES FOR RISK ANALYSIS OF FOODBORNE ANTIMICROBIAL RESISTANCE CAC/GL 77- 2011"	The Codex Standards are elaborated in consensus by member states with sound scientific base.
Recommendation C1, letter A	Add Education after advocacy	Education of the community in AMR and the prudent use of Antimicrobials should be included as part of a meaningful engagement ot only with civil society groups or organizations, within the whole community.
Recommendation E1 New letter	Create a member state contact point network to effectively	

communicate all the international	
efforts, resources, etc., to support,	
at national level, the AMR	
resistance challenge visibility in the	
Governmental agenda.	

Colombia

From: Elver Bejarano Gonzalez
To: IACG-secretariat
Subject: RV: Observaciones IACG

Date: Tuesday, February 19, 2019 22:37:38

De: Elver Bejarano Gonzalez

Enviado el: martes, 19 de febrero de 2019 04:35 p.m.

Para: 'iacg-secretariat@who.int' <iacg-secretariat@who.int> **CC:** 'Mariluz Villamil Sandoval'; Carlos Alberto Robles Cocuyame

Asunto: Observaciones IACG

Nombre: Elvert Bejarano Gonzalez

Título: Médico Veterinario, Esp. en Epidemiología.

MSC Inocuidad de Alimentos.

Institución: Instituto Nacional de Vigilancia de Medicamentos y Alimentos – INVIMA – Colombia.

Retroalimentación/

En los ítems

- ✓ Fortalecimiento de los mecanismos de nacionales de vigilancia, regulación y rendición de cuentas.
- ✓ Fortalecimiento de sistemas nacionales clave para la prevención de infecciones, monitoreo, la vigilancia integrada, la adquisición de productos de salud y la gestión de desechos.

Tener en cuenta en estos ítems del documento que:

Dado la complejidad del ciclo de los patógenos multiresistentes y sus determinantes genéticos, los sistemas nacionales deben conocerlo y entenderlo previo al diseño de sus sistemas de monitoreo y vigilancia, pues son la base para establecer medidas de control o intervenciones; además un aspecto clave en cada país es contar con las capacidades institucionales al planear una acción efectiva y sostenida para abordar la resistencia antimicrobiana según las necesidades de cada región.

Cordialmente.

ELVERT BEJARANO GONZALEZ Profesional Especializado Dirección de Alimentos y Bebidas

Colombia – unofficial translation

Name: Elvert Bejarano Gonzalez

Title: Veterinary Doctor, Expert in Epidemiology.

MSC Food Safety.

Institution: National Institute for Food and Drug Surveillance - INVIMA - Colombia

Feedback

In the items:

- Strengthening of national mechanisms for surveillance, regulation and rendering of accounts.
- Strengthening of key national systems for the prevention of infections, monitoring, integrated surveillance, procurement of health products and waste management.

Take into account in these items of the document that:

Given the complexity of the multiresistant pathogen cycle and its genetic determinants, national systems must know and understand it prior to the design of their monitoring and surveillance systems, since they are the basis for establishing control measures or interventions; In addition, a key aspect in each country is to have the institutional capacities to plan effective and sustained action to address antimicrobial resistance according to the needs of each region.

Feedback from the European Commission on the draft recommendations of the Ad hoc interagency Coordination Group on Antimicrobial Resistance

The European Commission welcomes the draft recommendations from the Ad hoc interagency Coordination Group on Antimicrobial Resistance (IACG) and to strengthen coordination to reduce the threat of AMR. We are pleased to see the One health approach to antimicrobial resistance cutting across human, terrestrial and aquatic animal and plant health as well as food production and the environment is well reflected throughout the document. We also share the importance of phasing out the use of antimicrobials for growth promotion.

We support the need to accelerate the response to Antimicrobial Resistance (AMR), in particular by ensuring all countries have developed and are implementing One-Health National Action Plans across human, animal, plant health and the environment. We strongly promote enhanced and effective infection prevention and control through better hygiene, vaccination and early detection and we consider that investment in research and collaboration of existing research networks needs to be increased.

In particular, we strongly welcome the suggestions made under Recommendations D1 on applying an "AMR one-health lens" to investments made through international financial funding instruments. We agree that, AMR considerations should be mainstreamed in funding flows. Given the important threat to health security posed by AMR, we should not only seek to mobilise all relevant possibilities for investment in combatting this threat, but should also ensure that whenever investments are made to advance development, , that those do not undermine global efforts to combat AMR. Instead, any investments in human health (including in the context of universal health coverage), animal health, including agriculture and food production, and the environment should continue to safeguard and promote the main tenets of the response against AMR, such as prudent use of antibiotics, enhanced infection protection and control, increased awareness-raising and better hygiene. Future decisions on investment need to be made "AMR-proof" and AMR-related criteria need to be integrated in official eligibility criteria for funding.

Regarding recommendation E1 on the creation of a Global Leadership Group on Anti-Microbial Resistance, we support the creation of such a group under the direct auspices of the UN Secretary-General. We share the view of the IACG that antimicrobial resistance should be addressed with greater urgency and that such a Leadership Group can help spearhead momentum and further raise awareness at highest levels for the need for action through a One Health approach. Such a Leadership Group should further explore the possibility for setting and working towards global targets on AMR – a topic that seemed to have been part of the IACG's mandate, but which the IACG has not picked up in its recommendations and has not provided further discussion. Similar to other areas (e.g. under the SDGs), the possibility for targets as a policy measure – either binding or voluntary – to push for change and guide efforts should be explored more prominently in global fora.

We are also convinced that greater emphasis should be put on the need to raise global awareness about AMR. Elements pertinent to this can be found in several recommendations (cf. Recommendation A1, C1, E1); however, this point could even merit a separate recommendation on its own.

AMR is a serious threat that is still not general knowledge for many people, and nowhere near the levels of general knowledge about particular diseases (e.g. HIV, influenza, etc.). Yet it is already claiming lives on a scale similar to some of them. For example, in the EU, the deaths from resistant infections was estimated at 33 000 people per year and the burden of these infections is comparable to that of influenza, tuberculosis and HIV/AIDS combined. Global bodies, such as the UN, as well as individual national actions should prioritise awareness raising for AMR, including what everyone can do to combat it, through education, health promotion and professional training for healthcare professionals, such as doctors, nurses and pharmacists.

Comments in more detail:

Page 3, box on Recommendation A1:

The question of access to antimircrobials is a difficult one. As it is important that patients have access to antimicrobials, too easy access, however, can lead to triggering the overuse of antimicrobial. Available antimicrobials should ensure treatment (so that there are fewer diseases, which should translate into less usage of antimicrobials), avoiding purchase of bad/fake products on the web etc.

A1. b.

- (Please add) "and through strengthening..." to make sure that both approaches are identified as separate lines of action.
- "infection prevention and control measures". (Please add) ", starting with improved hand hygiene" to highlight one simple effective and cost-effective intervention that would accelerate progress.

A1. d.

Properly placed incentives have shown to be effective in reducing inappropriate use of antibiotics and AMR. "incentives" is therefore an important point that would certainly accelerate progress and this point should be developed further, possibly as an independent bullet point separately from effective communication.

A1. e.

"developing national instruments" is the core of the recommendation and not just a supporting activity. Governance at a national level could be further highlighted, especially in terms of accountability, target setting, monitoring and implementation.

"Waste management" is mentioned twice, in c and in e, a consolidation should be considered

Page 4,

First para:

There is little emphasis on "stewardship" in the draft recommendations. The establishment of antimicrobial stewardship programmes in healthcare to promote the prudent use of antimicrobials is an effective and cost-effective intervention.

The document could reinforce the issue of education/stewardship and other options than antimicrobials (e.g. vaccines etc.) maybe in a special section.

3rd bullet point "establishing anti-microbial production facilities": Putting vaccines in the same basket as antimicrobials, may create confusion.

4th sub-bullet "providing affordable access": It is not always clear what is meant under drugs, if it covers antimicrobials or not, and this may create confusion: last paragraph at page 4 and first one at page 5 are not very clear as regards whether prescription only is a must or not. Sale over the 'over the counter' or the internet is normally open. Stricter rules should be applied.

Second para:

About "(...) veterinary paraprofessionals may also be trained and authorised to prescribe or administer **some** antimicrobial agents.": how would those antimicrobials allowed to be administered by paraprofessionals be defined, on which basis and by whom should it be decided? For your information, in the context of the new Regulation (EU) 2019/6 on veterinary medicines, which will apply as of January 2022, only veterinarians will be allowed to prescribe antimicrobials.

Page 5, box on Recommendation A2:

A2. b.

"infection prevention" includes both "vaccination" and "hospital hygiene/infection prevention and control in healthcare". Both are important and should be mentioned separately.

A2 c:

Technical cooperation support for champions at (please add) "international", national and local levels...

Page 6, box on Recommendation A3:

A3. "...to phase out the use of antibiotics for growth promotion... starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents..."

Please add "for growth promotion, for prevention of infections in group of animals or via medicated feed"

Page 6, Recommendation A3, third bullet point:

Same as above, i.e. "for growth promotion, for prevention of infections in group of animals or via medicated feed" (rather than just "for growth promotion")

Page 7, box on Recommendation B1:

B1. "...investment in new antimicrobials...":

By "new antimicrobials", the IACG most probably means novel antimicrobials active against prevalent multidrug-resistant organisms (not just any new antimicrobial compound), but this should be made more clear in this recommendation.

Implementation research, behaviour change research as well as quality improvement interventions are also important and should be mentioned.

More funding mechanisms should be created to boost R&D in animal health to counter AMR, not only through the development of new antimicrobials or vaccines, but also by defining innovative and smart approaches to livestock management.

Recommendation B1 b:

Building upon existing Product Development Partnerships (PDP) in human health and (please add) "possibly" establishing more of them, particularly for terrestrial and aquatic animal and plant health.

N.B. At the moment, there is just one PDP for AMR, GARD-P. In our view, there is no immediate need for another one. The development pipeline for new antimicrobials is weak, so more PDPs would not make much sense. It is very likely that any new antimicrobial that would successfully exits development will be reserved for human treatment. The situation regarding animal health will probably mostly benefit from improved animal husbandry practices and maybe from alternative treatments, that are still far from the market. An exception could be animal vaccine and diagnostics development.

In the 4th bullet point, the last sentence:and to (please add) "possibly" replicate them in terrestrial and aquatic animal and plant health.

Recommendation B3 a:

Undertaking coordinated global mapping of research and development activities and funding to address AMR

Note that a coordinated global mapping is already being performed by JPI AMR and the Global AMR R&D hub. Therefore, the recommendation might be changed into: Supporting coordinated global mapping of research and development activities and funding to address AMR

The first bullet point states "However, it emphasises that lack of information, collaboration and transparency across different research and development activities, funding agencies and partners continues to act as significant barriers to advancing research and development on AMR." This does not seem to take into account the most recent developments. The activities of the Global AMR R&D hub have just started and will specifically address this issue. Furthermore, the Virtual Research Institute of the JPIAMR is just starting and is expected to make major improvements here. The text could therefore be changed into: "It emphasises that efforts of the Global AMR R&D hub and JPIAMR to address the lack of information, collaboration and transparency across different research and development activities, funding agencies and partners should be supported in order to remove significant barriers to advancing research and development on AMR."

Recommendation D2:

Second bullet point "....such as JPIAMR, which is supported by 27 Member States and European Commission, as well as the Fleming fund of the UK government...."

Recommendation E2: on convening an Intergovernmental Panel on Evidence for Action against Antimicrobial Resistance.

We underline the need for good scientific evidence and surveillance as underlying foundations for effective response,

However, the proposed independent panel should not duplicate the work already done or ongoing at regional level and at the WHO AMR secretariat. It should instead collect and try to coordinate those activities at global level. It is unclear who will draft the mandate and the concrete issues this panel should explore.

Page 18, last line:

The current overlap between the Access and Watch categories and the absence of categorisation of several antibacterials which prevents use of the WHO Access/Watch/Reserve (AWaRe) classification for surveillance and monitoring antibiotic stewardship efforts. The WHO AWaRe classification should therefore urgently be reviewed and revised so it applicable for the above mentioned uses.

19 February 2018

FINLAND'S COMMENTS IN THE PUBLIC CONSULTATION ON THE DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE

Finland thanks the Interagency Coordination Group for the possibility to comment its draft recommendations. At this stage, Finland wishes the present the following comments, which represent the coordinated view of the Ministry of Social Affairs and Health, Ministry of Agriculture and Forestry, Ministry of the Environment, National Institute for Health and Welfare, the Finnish Food Authority and the National Expert Network for Prevention of antimicrobial resistance.

General observations

Finland welcomes the work of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance and takes note of the draft recommendations for approaches needed to ensure sustained effective global actions to address antimicrobial resistance.

The report presents thorough analyses of the issues and proposes guidelines on the way forward. However, Finland notes that the IACG's mandate is to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance. Additional practical guidance, ambitious enough and covering the entire span on necessary actions, as appropriate and where feasible, would be welcome.

"Accelerate progress in countries"

Finland welcomes the **recommendation A1** for all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health. Access to affordable, quality assured antimicrobials all over the globe is a very important goal.

As stated in the **recommendation A2**, the minimum requirement for all Member States should be the development and implementation of a One Health National AMR Action Plan that covers actions across all relevant sectors. In addition, implementation of an infection prevention program, and partnership of the WHO GLASS system would be beneficial steps.

Finland strongly supports phasing-out the use of antimicrobials for growth promotion (**recommendation A3**) starting immediately from HPCIAAs. It is important to do this so as not to increase the prophylactic/metaphylactic use of antimicrobials or to deteriorate animal health. Significant efforts are needed to improve the management and preventive measures in animal husbandry and aquaculture.

It should be noted that the world food economy has been increasingly driven by the shift of diets and food consumption patterns towards livestock products (World agriculture: towards 2015/2030, Summary report, http://www.fao.org/docrep/004/Y3557E/Y3557E00.HTM; http://www.fao.org/docrep/005/y4252e/y4252e05b.htm). Over the past 50 years, global meat production has almost quadrupled from 84 million tons in 1965 to more than 330 million tons in 2017 and the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD, World Agriculture Report), predicts that this trend will continue (https://www.globalagriculture.org/report-topics/meat-and-animal-feed.html). This trend has an impact on the use of growth promoters and should be taken into account when evaluating the use of growth promoters.

"Innovate to secure the future"

Finland welcomes investments and innovations not only in new antimicrobials but also in more accurate diagnostics and better preventive tools, such as vaccines, waste management tools, and safe and effective alternatives to antimicrobials (**recommendation B1**). We recall the need for prudent use of new antimicrobial agents as well as the old ones, where the continuous training of health professionals and access to diagnostics are essential.

We fully support the **recommendation B2** on the need for existing and future global access initiatives to promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

Finland supports the **recommendation B3** which calls upon all relevant stakeholders to strengthen research collaboration in a One Health context, for instance by sharing information on research. We stress the need for basic research and the innovation potential of research and development carried out by academia and small and medium sized enterprises. Moreover, we suggest this statement to be aligned with the Sustainable Development Goals, taking into consideration also other relevant international agreements and ongoing discussions on this field, such as the Nagoya protocol and the public health implications of its implementation. Finland strongly supports openness and transparency of data in connection with research, monitoring and surveillance.

"Strengthen accountability and global governance" (recommendations E1-E4)

Finland agrees with building and maintaining the political momentum and public support for global actions to address antimicrobial resistance. We also support efforts for more comprehensive monitoring of science and evidence related to antimicrobial resistance as well as more coordinated actions to tackle the problem. However, we also see value in building on existing governance structures and processes that are best placed to coordinate the work on AMR.

To form a position, Finland needs more information and an analysis on pros and cons on the proposal to establish a One Health Global Leadership Group supported by a secretariat. We would particularly appreciate information on how this initiative is related to the more coordinated actions by FAO, OIE, UNEP and other UN agencies.

19/02/2019

Comments from France on the document "Draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance – January 2019"

All comments from France are in bold in this document.

Page 3:

A. ACCELERATE PROGRESS IN COUNTRIES

The recommendations should insist on the "public awareness, behavior change, and communication" aspects. It is crucial in countries where antibiotics can be bought without prescription and where there are no regulations in agriculture. This aspect is crucial and needs to be reinforced. It is important to decrease the inadequate practices of health care professionals and to change the population or patients' behavior toward the use of antimicrobials.

A general and essential point here is coordination. Already a lot of activities are taking place in assisting national administrations, institutions, hospitals, etc. in mounting an adequate response to the AMR problem, coming from various public, private or international funders. There is a need to ensure proper coordination of all these activities so as to avoid dissemination, dilution and fragmentation of the responses, and increase synergies.

Recommendation A1: The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health.

France would like to add diagnostics in this recommendation because many people do not have access to diagnostics tests of ARM in low and middle income countries (LMICs). It is also essential to underline the urgent need of new standardized diagnostic tests to detect antibiotic resistance with a minimum of experiments, easy to implement, and affordable, particularly in LMICs that suffer from the lack of efficient detection in order to do adequate treatment prescriptions.

France suggests to clarify point e as follow:

A1-e. Developing national **process and** instruments based on international standards **so as to support** equitable access to and prudent use of existing and new quality-assured antimicrobials in humans, animals, plants and food production, as well as waste and water management in health care, manufacturing and farming-related activities;

Considerations for this recommendation:

Lack of updated essential medicines list and variable regulatory pathways in and in between countries are significant barriers in access to essential antimicrobials and should be identified as such in the document.

Suggestions to add to the existing list:

- Updated national list of essential antimicrobials to guide procurement activities on priority products and adequate presentations and formulations
- Harmonized regulatory pathways for antimicrobials and vaccines so as to avoid the existing complexity in terms of registration and commercialization resulting from divergence in approval requirements and processes. A global regulatory pathway would be helpful to support such harmonization

Page 4:

In the paragraph:

o Establishing antimicrobial production facilities: ...

Governments should ensure that the active principles that are incorporated in the drugs they deliver marketing authorisation to are manufactured respecting environmental standards".

This comment also applies to Recommendation C2.

Page 5:

In the paragraph:

 The IACG emphasizes that there is an urgent need Surveillance systems should include a set of specific indicators to enable monitoring of access, availability and affordability of antimicrobials and related commodities.

The IACG should ensure that these indicators are properly defined, standardized and disseminated for wide use and coordinated reporting and monitoring.

Page 6:

Recommendation A2: The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs that, at a minimum, include:

Considerations for this recommendation:

In the paragraph:

• The IACG emphasizes that One Health integrated surveillance and monitoring systems need to be established, coordinated and integrated, ...

Suggestion of clarification:

France supports this consideration for recommendation. However, clarification on how this will be operationalized needs to be provided.

Recommendation A3: The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotics Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins).

France suggests that this recommendation also focuses on the use of antibiotics in agriculture for prevention - not only as growth promoters. The number and the type of antibiotics used in low and middle income countries for prevention is indeed a public health issue.

Page 7:

B. INNOVATE TO SECURE THE FUTURE

Considerations for this recommendation:

In the paragraph:

• The IACG recognizes the need to develop and provide financial ...

Suggestion of clarification:

Could the IACG contribute to define the TPP with the help of an experts ad hoc group?

Page 8:

In the paragraph:

• The IACG recognizes that beyond product development, funding is also required for implementation and operational research, ...

This is a key point, as it deals with short-term research that can be undertaken relatively easily at country and regional levels, and can yield powerful information so as to assist governments and institutions to improve the fight against AMR through well targeted activities. This type of implementation/operational research MUST be undertaken while larger efforts are being invested to develop new diagnostics, medicines and vaccines. It should therefore appear in the recap box above that only deals with research on product development.

There is a need for guidance on how donors could optimize their investment in AMR which is not highlighted in the present document though this topic is quite extensively addressed by subgroup 3 discussion paper (*Invest in innovation and research, and boost R&D and access*). Such guidance would need to cover the following (1) identify priority needs due to market failure; (2) identify relevant instruments along the R&D value chain; (3) reflect on options to coordinate those mechanism at national, regional and global level.

Consequently, France suggests adding an additional recommendation to B that could be introduced between B1 and B2 as follow:

B2. The IACG recommends coordinated work to be undertaken to guide and optimize funding for priorities

- Basic research and clinical development of new antibiotics, specific diagnostics, vaccines and alternatives where there is market failure should be identified and prioritized by public funding
- Well-designed push and pull incentive mechanisms along R&D cycle should be identified/documented. Such incentives should facilitate "delinkage" (i.e. disconnecting the cost of investment in R&D form the expected price and volumes of sales) mechanisms which has been supported by the UNGA and G20.
- Coordination among global, regional and local level in designing and implementing such instruments should be secured.

Recommendation B2: The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

The question must be posed of the opportunity to create once more *new global initiatives* - when so many do already exist, with ensured funding. The risk is of an 'overcreation' of institutions and bodies, leading to competition for funding at national, regional and international levels. One

should consider how the already existing Initiatives (such as the ones cited in the bullet point above) could be approached and see their mandate expanded so as to include access to AMR-targeted products. This could be preferably done under the leadership of an oversighting body such as the one proposed at the end of these recommendations.

Page 10:

C. COLLABORATE FOR MORE EFFECTIVE ACTION

Suggestion of reformulation:

Aim of the recommendations in this section: While multisectoral efforts involving all stakeholders are essential to tackle the many challenges posed by antimicrobial resistance, the engagement of civil society and the private sector in the response is inadequate. These recommendations aim to strengthen the systematic engagement of these non-state stakeholders to optimize their contributions to the response to antimicrobial resistance, including working with governments.

Page 12:

D. INVEST FOR A SUSTAINABLE RESPONSE

Recommendation D1: The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and One Health "lens" when making investments through:

Suggestion of reformulation:

« Recommendation D1: The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and One Health "lens" when making investments and when appropriate through:».

France supports this recommendation but wants to emphasize the fact that this lens cannot be applied to all investments.

Suggestion of clarification:

<u>D1-c.</u> France would like to know why only IDA is mentioned.

Page 14:

E. STRENGTHEN ACCOUNTABILITY AND GLOBAL GOVERNANCE

General comments and suggestions:

- France supports the IACG's recommendations in this section which aims at proposing a global architecture on the fight against AMR.
- France would like the IACG to provide a conceptual framework to better understand the aim, actions and links of all initiatives and stakeholders from the above proposed One health Global Leadership Group on AMR to the National Action Plans on AMR.

Recommendation E1: The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat, to:

France would like the IACG:

to clarify the source of funding of the secretariat of this group.

- to explain how this group will integrate the existing initiatives on AMR such as GLASS, Global AMR R&D Hub, JPIAMR, JAMRAI, EARS-Net etc...

<u>E1-e:</u> France would like the IACG to clarify the formulation as it creates confusion on the respective role of the Group and the independent panel, especially to clarify that there is no hierarchical link between both.

<u>E1-g and h</u>: this is the role of Global AMR R&D Hub so the Hub needs to be mentioned and recalling that these 2 points are fulfilled by the Hub.

The platform needs to be closely connected to the strengths working on-site especially in the high AMR burden countries. The numerous research organizations that are working on AMR in LMICs can help for the implementation of "one health projects" but also identify the specific gaps in the different regions of the world that can vary according to the context. It is pertinent to connect these organizations to the "One Health Global Leadership Group on Antimicrobial Resistance» so as to utilize their expertise and coordinate their actions. This could help creating more concerted actions between these organizations.

Page 15:

In the paragraph:

• The IACG reiterates the urgent need to develop a shared global vision, narrative and targets to tackle antimicrobial resistance ...

France believes that this is the KEY message and the logic development of all recommendations described in this document. These recommendations will be confronted to multiple questions on the various means of implementation in a rational, efficient and coordinated way. This requires a shared global vision that the proposed group can develop, and that will determine the needed activities to be undertaken at the various national, regional and international levels, as well as the means to fund, monitor and value these activities.

Page 16:

Recommendation E2: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO,OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impact and future risks, and recommend options for adaptation and mitigation.

France believes that this Independent expertise panel is key to provide undisputable evidence on needs and achievements and would very usefully advise the leadership group proposed above.

Recommendation E3: The IACG requests the Tripartite agencies (FAO, OIE and WHO) together with UNEP and other UN agencies, in the context of the UN reform, to further strengthen joint One Health action, based on country priorities and needs, by enhancing their organizational capacity and providing adequate and sustainable core funding for antimicrobial resistance-related activities in order to:

Suggestion of reformulation:

E3-a: Integrate antimicrobial resistance-related activities into country UN Development Assistance Framework when appropriate;

E3-e: Guide, support; monitor and evaluate implementation, including on infection prevention and control, antimicrobial stewardship, integrated surveillance, data quality and harmonization, risk assessment, and demand forecasting and supply management

France supports the conduct of Joint Periodic Review missions on AMR and proposes that this reviews guide the National Action Plan on AMR as done with JEE and National Action Plans on Health Security.

Page 17:

Considerations for this recommendation:

Suggestion of clarification:

In the paragraph:

• The IACG recognizes of national action plans. : replace "Stewardship and prudent use" by "antimicrobial stewardship promoting prudent use".

Page 18:

Recommendation E4: The IACG recognizes the ongoing process led by Member States to develop the Global Development and Stewardship Framework to Combat Antimicrobial Resistance and urges the Tripartite agencies (FAO, OIE and WHO) and UNEP to expedite its development in line with the scope described in the 2015 World Health Assembly resolution on antimicrobial resistance (WHA68.7) . As Member States finalize this process, they should also consider the need for new international instruments.

Suggestion of clarification: France wants to emphasize that before considering new international instruments (especially binding instruments), it is necessary to ensure effective implementation of current initiatives (the Global Development and Stewardship Framework (GDSF) to Combat Antimicrobial Resistance for example), and review and evaluate existing recommendations (WHO, OIE, FAO, etc.) and mechanisms. Recommendation E4 of this report should thus solely concentrate on the development of the GDSF and not consider other alternative instruments at this stage.

Gabon

From: <u>carine mbadinga</u>
To: <u>IACG-secretariat</u>

Subject: commentaires GABON projet de recommandation du groupe spécial de coordination interinstitutions sur la

résistance aux antimicrobiens

Date: Tuesday, February 26, 2019 08:58:18

Dr MBADINGA MBADINGA Carine Géralde

Direction de la Pharmacie et du Médicament du GABON

Bonjour Monsieur, Madame,

veuillez trouver ci-joint les commentaires du comité de lutte contre la RAM concernant le projet de recommandation du groupe spécial:

<!--[if !supportLists]-->A. <!--[endif]--> ACCÉLÉRER LES PROGRÈS DANS LES PAYS

Recommandation A1: le Groupe spécial appelle tous les États Membres à garantir un accès équitable et abordable à des antimicrobiens existants ou nouveaux de qualité garantie, et leur utilisation prudente par des professionnels compétents et agréés dans l'ensemble des secteurs de la santé humaine, animale et végétale.

Cette recommandation doit être soutenue par des efforts visant à la fois à réduire le besoin en antimicrobiens et à améliorer l'accès moyennant :

- a. la réduction de la prévalence des infections par l'accès à l'eau potable, à l'assainissement et à l'hygiène ;
- b. la diminution du risque de maladies <u>infectieuses</u> et de leur propagation moyennant l'administration des vaccins existants et le renforcement des mesures de prévention et de lutte contre les infections;
- c. le respect des bonnes pratiques dans les domaines de la santé des animaux et des végétaux terrestres et aquatiques, de la production alimentaire et de la gestion des déchets;
- d. le soutien à un changement de comportement moyennant une communication efficace et des mesures d'incitation destinées au grand public et aux professionnels dans les domaines de la santé humaine, des animaux et des végétaux terrestres et aquatiques, de la production alimentaire et de l'environnement;
- e. l'élaboration d'instruments nationaux reposant sur les normes internationales pour l'accès équitable à des antimicrobiens existants ou nouveaux de qualité garantie, et leur usage prudent chez les humains, les animaux et les végétaux et dans la production alimentaire, ainsi que pour la gestion des déchets et de l'eau dans le cadre des soins de santé et des activités liées à la fabrication et à l'exploitation agricole; et

- f. le renforcement des mécanismes de surveillance, de réglementation et de responsabilisation au niveau national.
- g. Mettre en place un mécanisme approprié de gestion des dechets en tenant compte des mécanismes internationaux. (argumentaire : la gestion des déchets reste un problème et n'a pas de cadre juridique, il faut donc un alinéa spécifique. La gestion des différents déchets doit être gérer de manière concertée)

Recommandation A2: Le Groupe spécial appelle tous les États Membres à accélérer l'élaboration et la mise en œuvre de plans d'action nationaux pour combattre la résistance aux antimicrobiens suivant le principe « Un monde, une santé », dans le contexte des ODD, incluant au minimum:

- a. des mesures et des interventions prioritaires qui sont adaptées au contexte national, dont les coûts sont établis et financés, y compris moyennant l'allocation de ressources nationales suffisantes ;
- b. le renforcement des systèmes nationaux essentiels pour la prévention, le suivi et la surveillance intégrée des infections, l'achat des produits de santé et la gestion des déchets;
- c. la coopération technique, le renforcement des capacités, des éléments relatifs à la recherche et à la sensibilisation, y compris le soutien, aux niveaux local et national, aux champions de la mobilisation pour combattre la résistance aux antimicrobiens; et
- d. des mécanismes efficaces de coordination, de responsabilisation et de gouvernance au niveau <u>national</u>.

E. RENFORCER LA RESPONSABILISATION ET LA GOUVERNANCE MONDIALE

Objectif des recommandations de cette section : un leadership et une sensibilisation plus solides et soutenus, ainsi qu'un discours et une vision plus énergiques au niveau mondial sont autant d'éléments nécessaires pour faire progresser la riposte mondiale à la résistance aux antimicrobiens. Ces recommandations favorisent la création d'une instance qui permettra de mieux faire connaître la résistance aux antimicrobiens et le caractère urgent de la lutte contre celle-ci, de susciter et de maintenir un élan politique et le soutien du public, de favoriser un suivi un suivi plus complet des données scientifiques et des données relatives à cette résistance, et de garantir la responsabilisation parmi toutes les parties

prenantes.

Le reste du document n'a fait l'objet d'aucun commentaire.

<u>N.B.</u>: Les éléments soulignés en rouge sont les différentes propositions d'ajout qui ont été faite par le comité de lutte contre la RAM.

Cordialement.

Dr MBADINGA

Gabon – unofficial translation

The underlined elements in red are the different additions proposed by the committee against Antimicrobial resistance

A1b (in French version): Decreasing the risk of infectious diseases and their spread by the uptake of existing vaccines and strengthening infection prevention and control measures.

A1d (in French version): Support for behavior change through effective communication and incentives targeted at the public and professionals in **human**, terrestrial and aquatic animals and plants health, food production and the environment.

Add new bullet: "A1g": Establishment of an appropriate waste management mechanism taking into account international mechanisms. (Argument: waste management remains a challenge and does not have a legal framework, so a specific paragraph is needed). The management of different waste must be managed in a concerted manner.

A2d (in French version): At national level should be added in the end of: d. effective national coordination, accountability and governance mechanisms at national level.

Recommendation E (in French version): The word "Suivi" should be deleted from the French version of the aim of the recommendation (line 5)

- Germany welcomes the revision of the draft recommendations taking into account the results of
 the first consultation round. In general, we agree with the guiding principles, and feel these
 should be kept in mind for any future global efforts to fight AMR. We broadly support the
 proposed recommendations, in particular the efforts to reduce the need for antibiotics, stronger
 involvement of other stakeholders, strengthening of the Tripartite plus and completion of the
 Development and Stewardship framework.
- Nevertheless, we miss a clear recognition of previous work of the Tripartite Plus and the WHO
 AMR secretariat. It is unclear how the IACG will consider their valuable experience for further
 proceeding. AMR Governance should be in the hands of the Tripartite Plus and the WHO AMR
 secretariat, which will need adequate technical and financial support.
- We also think that the draft paper makes a valuable contribution to AMR conceptually by highlighting, for example, the importance of strengthening existing systems and aligning AMR efforts with the Sustainable Development Goals (SDGs).
- The Global AMR R&D Hub established under the Germany G20 Presidency is well placed to fulfil the recommendations in section B3. As a first central deliverable, the Hub will develop a close to real-time Dynamic Dashboard, providing information and high level analyses on current initiatives, funding flows and activities in the field of AMR R&D. For the development of the Dynamic Dashboard and other activities, which necessitate the consultation of stakeholders, a Stakeholder Group will be implemented. Ad-hoc Expert Advisory Groups and thematic workshops will provide required special expertise to inform the work of the Hub. As the first of these activities a "Market Analysis Expert Advisory Group" will be established and a workshop on "Increasing investments for AMR R&D" will be conducted on the margins of the World Health Assembly and the G20 Health Working Group meeting in May 2019. From our point of view, the IACG recommendations should reflect the work of the Global AMR R&D Hub and advertise for increased support from other countries. Germany opposes the implementation of new legally binding coordination mechanisms for research and development in the field of antimicrobial resistance. We welcome the IACG's reference to the Tripartite Plus and UN Environment's draft Global Framework for Development & Stewardship to Combat Antimicrobial Resistance.
- The recommendations on funding and the proposed governance mechanisms remain problematic for Germany for several reasons. As mentioned in earlier comments, further governance should be taken on by the Tripartite plus and WHO AMR secretariat, and their role should be strengthened with regard to the One Health perspective. Additional structures would lead to a loss of synergies and will not bring the expected added value due to the fact that the need for coordination will increase. New responsible groups would need additional resources which are not foreseen.
- Recommendation E1 One Health Global Leadership Group: In our view, better coordination of global AMR activities is urgently needed. To this end, the implementation of the IACG recommendation on strengthening the internal structures of the Tripartite Plus will provide a

- valuable contribution. However, we see the creation of new groups that also require adequate funding critically. It has to be considered that the UNDS-Reform does not provide additional financing funds for the implementation of selected topics nor selected advisory groups.
- From our point of view, we are not sure if the monitoring of progress in the field of AMR is the right task for former heads of state and ministers, because the group needs global political acceptance and appropriate technical knowledge. AMR as a challenge for global health is more the task of acting heads of state and responsible ministers as well as the task of relevant political fora like G7 and G20. The Tripartite Plus and the WHO AMR secretariat should play a crucial role in this regard. We are not sure if the proposed composition of the group is actually the best solution.
- Germany is currently discussing and drawing up a proposal on possible alternatives for the
 proposed leadership group and governance mechanism. One major objective for a possible
 future AMR governance mechanism is to strengthen existing structures and avoid building up
 new structures for coordination and enforcement of measures. Germany will bring the results
 into the ongoing discussion.
- Recommendation E2 calls for an "Independent Panel on Evidence for Action against Antimicrobial Resistance". Although we see the value of having a body of experts that independently provides scientific advice and evidence on antimicrobial resistance, we do not see the need for the proposed new panel. On the contrary, we see added value in having expert advice at different levels to address different (national, regional, global) needs. Scientific and technical assessments already take place at member state level, WHO and other international organizations. With the STAG a suitable body already exists for the human sector at WHO at the global level. Similar bodies may also exist for the veterinary, agricultural and environmental sectors. An intensification of their activities as well as increased cross-sector cooperation of these committees seems to be expedient. Therefore, the support and the strengthening of the central role of the Tripartite Plus and the WHO AMR secretariat is even more important. Furthermore, we refer to our activities on the AMR governance mechanism.
- We agree that measures at both, national and global level, need to be adequately funded.
 However, the recommendations should take into account that this is primarily a national
 responsibility. Many countries have already developed funding mechanisms at national level
 and are also involved in funding at the global level. Mechanisms for the support of financially
 weak countries should be considered.
- The IACG's mandate is to provide "practical guidance" for ensuring effective global action to tackle AMR. We recognise the value of a short and concise document. However, we feel that in some areas of the document, such as section C "Collaborate for More Effective Action" there is detail lacking around practical suggestions for how the private sector can be positively engaged and what the terms of their engagement might be.

- Recommendation A1 and B2: Both recommendations take up the issue of access. The individual recommendations listed under A1 have, with the exception of "e." no effect on access. We propose for the sake of clarity, to address access under only one recommendation.
- Section B "Innovate to Secure the Future" (the financing and the development of new products)
 and section D "Invest for a Sustainable Response" (financing of AMR generally, including
 product development) could probably be combined. While we agree that sufficient funding,
 including for product development and the right mechanisms for this, are important, two
 separate sections do not seem necessary.
- We also notice that the draft makes very little reference to surveillance and monitoring. We believe that this warrants its own section or at least a prominent position in one of the other sections, such as in section C "Collaborate for More Effective Action". Surveillance and monitoring are an essential first step for planning suitable coherent and collaborative responses to the threat of AMR. This is still a major area for improvement for the majority of countries and remains a gap that the IACG can help to address. Furthermore, the report lacks reference to the 'WHO Report on Surveillance of Antibiotic Consumption' and to the 'Global Antimicrobial Resistance Surveillance System (GLASS)'. Countries should be encouraged to gather and provide data on a regular basis to inform these global surveillance instruments.
- We urge the IACG to engage low and middle income countries (LMICs) in conversations around their recommendations. We noted that there were no consultation responses from LMICs to the IACG's previous governance discussion paper. LMICs are likely to have different needs to those in high income countries (HICs), many of which relate to system issues., The voice of LMICs is essential for making sure that any next steps take the full spectrum of resources and needs into account, and that we have a genuinely global understanding of AMR and a globally agreed set of measures and actions.
- To summarise, we think that the IACG's paper includes some useful elements, such as the guiding principles and the link to the system aspects, such as the SDGs and systems strengthening. However, we would like to see the following considered for the final document:
 - o Consider where more practical suggestions could be included in the recommendations.
 - Review the way that the sections have been structured, whether these are the right areas of focus (for example, consider more attention to surveillance and monitoring), and the clarity and coherence of these.
 - Consider how existing frameworks, structures, initiatives, resources and capacities could best be capitalised for the future (for example, consider the structures of the WHO, the Tripartite Plus and UN Environment).
 - Address the importance of surveillance through the 'WHO Report on Surveillance of Antibiotic Consumption' and the 'Global Antimicrobial Resistance Surveillance System (GLASS)'.
 - Engage more with LMICs to ensure their active participation in and ownership of any globally agreed understanding and actions.

- o Review whether recommendation B3 relates to a gap that still needs addressing.
- Consider that the UNDS-Reform does not provide additional financing funds for the implementation of selected topics.

Japan

From: <u>Japan MHLW(whomhlw)</u>
To: <u>IACG-secretariat</u>

Cc: 内山 美友紀(uchiyama-miyuki); 東良 俊孝(higashira-toshitaka); 西澤 ^送晃(nishizawa-hideaki); 松村

KOIZUMI TAKATO; AKAHANE NAOKI; 井口豪(inokuchi-tsuyoshi); 繁本憲立(shigemoto-norifumi); 嶋田

聡(shimada-satoshi11); 柳川 愛寒(yanagawa-manami)

Subject: [IMPORTANT] feedback on the draft IACG recommendations

Date: Tuesday, February 19, 2019 11:20:09

Dear IACG Secretariat,

Thank you for providing us an opportunity to comment on the draft recommendations of the Ad hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance.

Please find following comments from the Ministry of Health, Labour and Welfare (MHLW) and the Ministry of Agriculture, Forestry and Fisheries (MAFF) of Japan.

- We appreciate the continuous efforts by the IACG to develop the draft recommendations for AMR.
- Regarding the Guiding Principles on page 2, MHLW and MAFF are convinced that in the effort of combating AMR, it is critically important that the relevant authorities and agencies collaborate closely without shifting blame among each other, which is referred to "no apportioning of blame" in the working principles of the IACG Work Plan agreed in 2017 after the public consultation. We consider it is desirable that this important principle be retained and mentioned in this final report.
- We support the draft recommendations from Section A to Section D, which conform with the WHO Global Action Plan. However, regarding A3, which is about phasing out the use of antimicrobials for growth promotion, we recognize that conducting appropriate risk analysis is important as stated in the WHO Global Action Plan and the OIE recommendations, as well as in the "Considerations for this recommendation" section of this report. It is desirable that this point be mentioned in the recommendation.
- We are of the opinion that more concrete scientific evidence is needed in order to assist Member States to implement their AMR National Action Plans. We also recognize that more collaborative actions as well as coorperations among the Tripartite organizations(OIE, WHO, FAO) are required in the context of One-Health approach. For the above reasons, we are supportive of recommendations E2 and E3.
- Regarding how to maintain the political momentum to combat AMR as stated in E1 and new international instruments which were recommended to be considered in E4, given that 1) there are other possible mechanisms to attain that purpose and 2) it is necessary to examine the effect of the efforts made by Member States in implementing measures in their AMR National Action Plans which were developed according to the Global Action Plan as well as the effect of the mechanism of the Tripartite organizations to support and monitor such efforts, we consider that there should be broad-ranging discussions beyond what are proposed in E1 and E4.
- We fully understand the importance of engaging in the various stakeholders other than Member States. At the same time, the governments of Member States play central roles in developing and implementing policies to control and monitor AMR with the support of the Tripartite organizations. Thus, the considerations should be given to this point when any discussion platform to be established.

Luxembourg

Propositions concernant le **Projet de recommandations du groupe spécial de coordination interinstitutions sur la résistance aux antimicrobiens** (janvier 2019)

Nous tenons à féliciter le Groupe spécial de coordination interinstitutions pour tout le travail en faveur de la lutte contre la résistance aux antimicrobiens.

Le projet de recommandations du groupe spécial sur la résistance aux antimicrobiens est soumis à discussion publique. C'est dans ce contexte que nous désirons formuler quelques propositions.

Propositions:

- 1. Dans l'ensemble du texte, remplacer « utilisation prudente » des antimicrobiens par « utilisation appropriée » ou « utilisation raisonnée » des antimicrobiens.
- 2. Page 2 : « Selon les estimations, les infections pharmacorésistantes sont d'ores et déjà à l'origine de 700 000 décès chaque année » ajouter dans le monde : « Selon les estimations, les infections pharmacorésistantes sont d'ores et déjà à l'origine de 700 000 décès chaque année dans le monde »
- 3. Page 4 : « d. le soutien à un changement de comportement moyennant une communication efficace et des mesures d'incitation destinées au grand public et aux professionnels dans les domaines de la santé des animaux et des végétaux terrestres et aquatiques, de la production alimentaire et de l'environnement » ajouter une éducation et santé humaine dans le texte : « d. le soutien à un changement de comportement moyennant <u>une éducation</u> et une communication efficace et des mesures d'incitation destinées au grand public et aux professionnels dans les domaines de la santé <u>humaine</u>, des animaux et des végétaux terrestres et aquatiques, de la production alimentaire et de l'environnement »
- 4. Page 4 : « Le Groupe spécial reconnaît que des systèmes efficaces de prévention et de lutte contre les infections, parmi lesquels la vaccination, l'eau potable, l'assainissement et l'hygiène, ainsi que de bonnes pratiques de gestion,... » ajouter éducation : «Le Groupe spécial reconnaît que des systèmes efficaces de prévention et de lutte contre les infections, parmi lesquels la vaccination, l'eau potable, l'assainissement et l'hygiène, ainsi que l'éducation, de bonnes pratiques de gestion,... »
- 5. Page 5 : « à des prix abordables » : une étude danoise (2010) montre un lien entre diminution du prix des antibiotiques/introduction des génériques et augmentation de leur consommation. Dans certains pays européens, le coût des antibiotiques a même été augmenté afin de limiter la surconsommation et le développement des résistances. L'évaluation du prix abordable devrait en tenir compte.
- 6. Page 6 : dans l'encadré « recommandation A2 » la fin de la dernière phrase manque « d. des mécanismes efficaces de coordination, de responsabilisation et de gouvernance au niveau »
- 7. Page 7: encadré « recommandation A3»: il y a comme une contradiction à vouloirs éliminer progressivement l'utilisation des antimicrobiens pour stimuler la croissance et le fait de mettre immédiatement un terme à l'utilisation des agents antibiotiques critiques. Proposition de reformulation « le Groupe spécial appelle tous les Etats Membres à éliminer l'utilisation des antimicrobiens pour stimuler la croissance, ... »

- 8. Page 12 : ajouter « de groupes de représentation de patients » dans le premier paragraphe des « Considérations relatives à cette recommandation »
- 9. Page 18 : «favoriser <mark>un suivi</mark> un suivi plus complet des données scientifiques » enlever un suivi
- 10. Page 19 : ajouter « des ministres de l'économie » et « la société civile » dans le dernier paragraphe

<u>Propositions regarding the draft recommendations of the Interagency Coordination Groupe</u> (January 2019)

We would like to congratulate the IACG group in their work on combating antimicrobial resistance. It's in this context that we would like to draw up some proposals:

- 1. We suggest that (Prudent use) must be replaced by appropriate use or reasonable use throughout the documents.
- 2. In Page 2, "Drug resistant infections are already estimated to cause at least 700,000 deaths every year. (in the world) should be added to the end of the sentence, "Drug resistant infections are already estimated to cause at least 700,000 deaths every year in the world".
- 3. In Page 4, education and human health must be added to the text in paragraph d: Supporting behavior change through effective **education** and communication and incentives targeted at the public and professionals in **human**, terrestrial and aquatic animal and plant health, as well as food production and the environment.
- 4. Page 4, education should be added to the following text: the IACG recognizes that effective systems for the infection prevention and control, including vaccination, clean water, sanitation and hygiene, as well as **education**, Good Management Practices....).
- 5. Page 5, "at affordable prices", a Danish study demonstrates the existence of a link between the decrease in the price of antibiotics/ introduction of generics and the increase of their consumption. In some European countries, the price of antibiotics has been raised to limit the over-consumption of antibiotics and the development of antibiotic resistance. The evaluation of affordable prices need to be considered.
- 6. Page 6, recommendation A2, d, high level should be added to : effective national coordination, accountability and **high level** governance mechanisms.
- 7. Page 7, recommendation A3, we would like to point out a contradiction between the progressive elimination of antimicrobials use and to put an immediate end to the use of antimicrobials use. We suggest the following reformulation of the first sentence: "The IACG calls on all Members states to eliminate the use of antimicrobials for growth promotion....".
- 8. Page 12, "Patient representation groups" must be added to the paragraph "considerations for this recommendation".

- 9. Page 18, remove follow up from the sentence "Encouraging follow-up follow up and more complete monitoring of scientific data".
- 10. Page 19, Add "Ministers of economy" and "civil society" in the last paragraph.

MALI PUBLIC DISCUSSION ON:

DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE

(For public discussion prior to finalization)

January 2019

Recommendation A1: The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health.

This recommendation must be supported by efforts both to reduce the need for antimicrobials and improve access through:

- Lowering the prevalence of infection through clean water, sanitation and hygiene;
- Decreasing the likelihood of diseases and their spread through delivery of existing vaccines and strengthening infection prevention and control measures;
- Ensuring best practices in terrestrial and aquatic animal and plant health, food production and waste management;
- Supporting behaviour change through effective communication and incentives targeted at the public and professionals in human, terrestrial and aquatic animal and plant health, as well as food production and the environment;
- Developing national instruments based on international standards for equitable access to and prudent use of existing and new quality-assured antimicrobials in humans, animals, plants and food production, as well as waste and water management in health care, manufacturing and farming-related activities; and
- f. Strengthening national surveillance, regulatory and accountability mechanisms.
 - Veuillez intégrer cette recommandation dans le cadre de la révision des Listes Nationales en Médicaments Essentiels (LNME) des pays concernés

Recommendation A2: The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs that, at a minimum, include:

- Prioritized actions and interventions that are specific to the national context and that are costed and funded, including with adequate domestic resource allocations;
- Strengthening key national systems for infection prevention, monitoring, integrated surveillance, procurement of health commodities and waste management;
- Technical co-operation, capacity development, research and advocacy components, including support for champions at national and local levels to mobilize action on antimicrobial resistance; and
- d. Effective national coordination, accountability and governance mechanisms.
 - ➤ Le décret One Health est effectif au Mali, les états devront s'accorder sur un format commun afin de faciliter la mise en œuvre.
 - > Le développement des capacités des laboratoires devra être prioritaire

Recommendation A3: The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins).

Les initiatives tripartites sont à encourager en ce qui concerne la RAM, il est à créer une structure de coordination/consolidaion des guides et outils communs aux trois agences (OMS, OIE et FAO).

Recommendation B1: The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials - particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials - for human, terrestrial and aquatic animal and plant health through:

- a. Financial and non-financial incentives strategically targeting the most important research and development needs, scientific challenges, and market barriers based on the principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance; and
- Building upon existing Product Development Partnerships in human health and establishing more of them, particularly for terrestrial and aquatic animal and plant health.
 - Mettre le focus sur la destruction des périmés et faux/falsifiés car source de contamination de l'environnement, des animaux et des humains, voire de réintroduction dans le circuit d'usage et de consommation.

Recommendation B2: The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

Rendre accessible les données sur la lutte contre la RAM sur des platformes digitales accessibles à tous.

Recommendation B3: The IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context by:

- Undertaking coordinated global mapping of research and development activities and funding to address antimicrobial resistance;
- Establishing and maintaining a platform for sharing information on research and compounds in development in both ongoing and completed research and development activities;
- Promoting synergies and opportunities for collaboration among funders and researchers in human, animal and plant health, and the environment; and
- Promoting openness and transparency in data from all research and monitoring and surveillance sources.
 - Elargir l'initiative One Health à d'autres types d'acteurs (célébrités du showbiz ; société civile etc...)

Recommendation C1: The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels through:

- Strengthening their roles in accountability, advocacy, monitoring progress and ensuring prudent use of antimicrobials;
- Promoting synergies with consumer and civil society groups active in other sectors, including in climate change and the environment, responses to HIV, TB and malaria, Universal Health Coverage and other aspects of the SDGs; and
- Provision of political, financial and technical support for civil society organizations to enhance their engagement, including for work with governments.
- Elargir l'initiative One Health à d'autres types d'acteurs (célébrités du showbiz ; société civile etc...)
- Ne pas omettre les approches communautaires

Recommendation C2: The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels in order to ensure:

- Affordable access, prudent use and stewardship of antimicrobials;
- Ethical production, distribution and marketing practices, including through environmentally sustainable production and waste management and the elimination of inappropriate incentives to sell antimicrobials;
- Engagement by the private sector in collaborative efforts to collect, analyze and use data and realign economic incentives to improve production, distribution and marketing practices; and
- d. Contributions to addressing antimicrobial resistance through testing of innovative approaches, corporate social responsibility, and similar initiatives.
 - Elargir l'initiative One Health à d'autres types d'acteurs (célébrités du showbiz ; société civile etc...)

Recommendation D1: The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and One Health "lens" when making investments through:

- a. Official Development Assistance;
- b. South-South cooperation;
- The International Development Association (IDA) replenishment process from IDA19 onwards;
- d. Financial support, grants, loans, credits and insurance for terrestrial and aquatic animals and plants, health, development, food systems, manufacturing of health products, the environment and other relevant areas.
 - Adapter les instruments de financement et d'aide international au contexte du One Health et de la RAM

Recommendation D2: The IACG emphasizes the need for increased investment in the global response to antimicrobial resistance. It urges existing and future financing mechanisms in human, animal and plant health, as well as food production and the environment - including Gavi — the Vaccine Alliance, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Global Financing Facility, Multilateral Climate Funds, Unitaid, as well as future financing streams for Universal Health Coverage and other priority development issues, and their donors - to give antimicrobial resistance greater priority in their resource allocations. It further calls upon public, private and philanthropic donors in human, animal and plant health, as well as food production and the environment, to increase funding to contribute to addressing antimicrobial resistance, including to support implementation of National Antimicrobial Resistance Action Plans.

Proposer la priorisation de la Ram dans le contexte One Health pour les mécanismes de financement au niveau Mondial.

Recommendation E1: The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat, to:

- Maintain urgency, public support, political momentum and visibility of the antimicrobial resistance challenge on the global agenda, and set targets;
- Advocate for action, including support for the expanding work of the Tripartite agencies (FAO, OIE and WHO), UN Environment (UNEP) and other international and regional entities;
- Monitor and report on progress, gaps and accountability in the global response to antimicrobial resistance;
- d. Expand multi-stakeholder engagement by establishing a partnership platform with the participation of Member States, UN agencies, international and intergovernmental organisations and regional entities, civil society, the private sector, researchers and other key stakeholders to develop and work towards a shared global vision and coordinated action on antimicrobial resistance;
- e. Provide advice and guidance on reports of the Independent Panel on Evidence for Action against Antimicrobial Resistance (recommendation E2);
- f. Monitor and advocate for the inclusion of antimicrobial resistance and a One Health "lens" in investments and programmes of major financing instruments for agriculture, health, development, food production and other relevant areas (recommendation D1);
- Identify priorities for research and development and facilitate implementation research in a One Health context; and
- Define the financial needs and gaps for the global response to antimicrobial resistance, including the costs of inaction and anticipated returns on investment.

> RAS

Recommendation E2: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.

> RAS

Recommendation E3: The IACG requests the Tripartite agencies (FAO, OIE and WHO) together with UNEP and other UN agencies, in the context of UN reform, to further strengthen joint One Health action, based on country priorities and needs, by enhancing their organizational capacity and providing adequate and sustainable core funding for antimicrobial resistance-related activities in order to:

- Integrate antimicrobial resistance-related activities into country UN Development Assistance Frameworks;
- b. Provide and update effective normative guidance, standards and tools when needed;
- Advise on priority evidence-based interventions and actions;
- d. Provide coordinated technical co-operation and capacity building, including One Health regional platforms for technical co-operation; and
- Guide, support, monitor and evaluate implementation, including on infection prevention, integrated surveillance, data quality and harmonization, risk assessment, and demand forecasting and supply management.

> RAS

Recommendation E4: The IACG recognizes the ongoing process led by Member States to develop the Global Development and Stewardship Framework to Combat Antimicrobial Resistance and urges the Tripartite agencies (FAO, OIE and WHO) and UNEP to expedite its development in line with the scope described in the 2015 World Health Assembly resolution on antimicrobial resistance (WHA68.7). As Member States finalize this process, they should also consider the need for new international instruments.

De nouveaux instruments et mécanismes de financement au niveau mondial sont attendus au sortir de ce rapport.

Mali - unofficial translation

- A1:
 - Please integrate this recommendation as part of the review of the National Essential medicines lists of concerned countries.
- A2:
 - The decree One health is effective in Mali. A common format needs to be agreed for all members states to facilitate its implementation.
 - Laboratory capacity development should be a priority.
- A3:
 - Tripartite initiatives on AMR should be encouraged, its necessary to create a coordination /consolidation structure of guides and tools common to the three agencies (WHO, OIE and FAO).
- B1:
- Emphasis on destroying obsolete and false/ falsified as a source of contamination of the environment, animals and humans, even the reintroduction in the circuit of use and consumption.
- B2:
- Make data on AMR accessible on digital platforms accessible to all.
- B3:
 - Extend the One health initiative to other types of actors (showbiz celebrities, civil society...etc.).
- C1:
- Extend the One health initiative to other types of actors (showbiz celebrities, civil society...etc.).
- Do not omit community approaches.
- C2:
- Extend the One health initiative to other types of actors (showbiz celebrities, civil society...etc.).
- D1:
 - o Adapt funding and international aid instruments to the context of One Health and AMR.
- D2:
 - o Propose AMR prioritization in the One Health context for global funding mechanisms.
- E1:
- Nothing to report.
- E2:
- Nothing to report.
- E3:
- Nothing to report
- E4:
- New instruments and financing mechanisms at the global level are expected when this report comes out.



Proyecto de informe de recomendaciones del Grupo ad hoc de Coordinación Interinstitucional sobre la Resistencia a los Antimicrobianos (IACG-AMR)

Comentarios del Gobierno de México

"Se considera que las recomendaciones de dicho Grupo reflejan asuntos importantes que deben ser abordados por los órganos de Naciones Unidas y otros foros a fin de mantener la coordinación interagencial contra la RAM/AMR.

En este tenor, se estima que el informe IACG debe servir como un diagnóstico que ayude a conocer los desafios que enfrenta la AMR e identificar cuáles son las áreas de oportunidad que se pueden abordar desde la perspectiva de cada grupo a fin de fortalecer la gobernanza y evitar la duplicidad de esfuerzos.

De esta manera, esta oficina coincide en las cinco áreas que se identifican como urgentes en el trabajo RAM/AMR, ya que es importante que todos los países continúen realizando esfuerzos en esta problemática; que exista una colaboración más efectiva y sostenible; y que se fortalezca la responsabilidad y gobernanza global, por lo que manifestamos total concordancia con lo que se establece en el rubro E1, relacionado con mantener el liderazgo y visibilidad del enfoque "Una Salud" en el abordaje del tema, desde una perspectiva de abogacía multilateral.

Por último, se considera que el informe IACG que se presentará ante la Asamblea debe incluir las recomendaciones que el grupo manifiesta sin modificar la esencia de los desafíos que se perciben; y que, por tanto, las observaciones o comentarios que los Estados Miembros realicen sean presentados como material adicional que contribuya a reforzar el contenido del documento sin alterar las recomendaciones que se mencionan en el proyecto. Asimismo, se estima conveniente alentar al IACG en reforzar el seguimiento y avance de las actividades que propone."

Mexico - unofficial translation

It is considered that the recommendations of this Group reflect important issues that must be addressed by United Nations bodies and other forums in order to maintain inter-agency coordination against AMR.

In this regard, it is considered that the IACG report should serve as a diagnosis to help identify the challenges faced from AMR and identify the areas of opportunity that can be addressed from the perspective of each group in order to strengthen governance and avoid duplication of efforts.

In this way, this office agrees with the five areas that are identified as urgent in work on AMR, since it is important that all countries continue to make efforts in addressing this problem; that there is a more effective and sustainable collaboration; and that the global responsibility and governance be strengthened. For these reasons we fully agree with what is outlined in section E1, related to maintaining the leadership and visibility of the "One Health" approach in addressing the issue from a multilateral advocacy perspective.

Finally, it is considered that the IACG report to be presented to the Assembly must include the recommendations that the group expresses without changing the essence of the perceived challenges; and that, therefore, Member States' observations or comments are presented as additional material that contributes to reinforce the content of the document without altering the recommendations mentioned in the draft. Likewise, it is considered advisable to encourage the IACG to strengthen the follow up and progress of the activities it proposes.

The Netherlands

The Netherlands response to the draft IACG recommendations

The Netherlands thanks the IACG for its work and is pleased to get the opportunity to reflect on the draft recommendations prior the finalization of the IACG report to be submitted to the Secretary General of the United Nations. The Netherlands is pleased that IACG recognizes a One Health approach as a guiding principle for its recommendations, as well as strengthening existing systems and mainstreaming efforts as guiding principle.

The draft recommendations form a solid basis for reporting to the Secretary General of the United Nations and create a good foundation for discussing and defining the next steps in accelerating our joint international efforts to tackle the problems of antimicrobial resistance globally.

The Netherlands fully agrees with recommendation to accelerate the development and implementation of the One Health National Action Plans. These Action Plans form the foundation of firm national action and there is a clear need for urging national governments to comply with the standards set in the Global Action Plan on AMR. Moreover, the Netherlands welcomes in this respect the call for cooperation and solidarity among all countries.

The Netherlands commends IACG for its stand on phasing out antimicrobials for growth promotors and starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents. WHO's guidelines on the use of medically important antimicrobials in food-producing animals is important guidance in achieving this. Moreover, the Netherlands would like to draw the attention of IACG to recent EU legislation (Regulations on veterinary medicines and medicated feed) in this field as good practice.

IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health. However, the Netherlands is of the opinion that future antibiotics, in relation to global access initiatives, should be developed for human use only.

The Netherlands welcomes the IACG recommendations that relate to strengthening the Tripartite cooperation, because strong cooperation by the Tripartite is the backbone of delivering effective assistance to member states' efforts to develop and implement the National Action Plans.

The Netherlands welcomes the recommendations that emphasize the need to incorporate AMR as an important element in Official Development Assistance. The fact that AMR threatens the achievement of all health related SDGs is an important notice. From sustainability point of view, we think it is crucial that AMR is seen as part of the UHC discussion, and not treated as 'yet another health issue'

The global (knowledge) agenda on AMR needs a boost. The Netherlands takes note with interest of the proposal of IACG to establish a One Health Global Leadership Group and an independent panel. The Netherlands requests IACG to clarify more clearly in its final report how these new entities will function in relation to the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations.

The IACG acknowledges the current debates and discussions about binding or non-binding international instruments to combat antimicrobial resistance and recognizes the enormous challenge of developing and negotiating such international instruments among Member States.

The IACG recommends that priority should be given to adopting and implementing global standards and best practices established by the Tripartite agencies (FAO, OIE and WHO) and other international and national authorities, and that the current debates and discussions should not distract from this priority. The Netherlands agrees with this notion. However, in relation to the recommendation to develop the Global Development and Stewardship Framework to Combat Antimicrobial Resistance and its call to Member States to consider the need for new international instruments, the Netherlands would like to firmly suggest the IACG to further elaborate on its own view on this need as well. As long as national policies do not only affect the national situation, but global health as well, we feel there is a need for UN agencies to take responsibility for the sake of global good. We would like to know what level of accountability the IACG considers necessary to ensure a minimum level of implementation at country level.

New Zealand

From: on behalf of

To: IACG-secretariat

Cc: Allan Kinsella; ; Warren Hughes;

Subject: New Zealand Feedback - Draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial

Resistance

Date: Tuesday, February 19, 2019 04:09:16

Dear Ad hoc Interagency Coordination Group on Antimicrobial Resistance Secretariat,

New Zealand supports the approach of the Ad hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance (AMR) and its recommendations, in particular the focus on:

- equity;
- · strengthening existing systems; and
- addressing key gaps and bottlenecks in the current response to AMR.

We have the following specific comments for consideration of the IACG:

- Page 14-15: if the One Health Global Leadership Group on AMR is established to continue efforts
 of the IACG, we encourage careful consideration of monitoring and reporting frameworks. This
 should ideally include how they link to World Health Organization, Food and Agricuture
 Organization and World Organisation for Animal Health reporting, as well as the Sustainable
 Development Goals, aiming to make monitoring and reporting as efficient and useful as possible
 for countries.
- Page 16: we support establishment of an Independent Panel on Evidence for Action against AMR.
 We suggest this includes experts who can provide a policy and implementation lens to ensure evidence and options posed for mitigation or adaptation are feasible and meaningful at the national level.
- Page 17: rather than developing a new Joint Periodic Review mission model specific for AMR, we suggest considering enhancing the Joint External Evaluation Technical Area on AMR to fulfil this purpose.

Sincerely,

Deborah Woodley Deputy Director-General Population Health and Prevention Ministry of Health, New Zealand

and

Allan Kinsella Acting Deputy Director-General Regulation and Assurance Ministry for Primary Industries, New Zealand

Draft Recommendations of the Ad hoc InterAgency coordination group on AMR

Comments from Norway

Norway is pleased to have the opportunity to provide comments to the IACG draft recommendations. Comments are submitted on behalf of the following five Ministries; Ministry of Agriculture and Food, Misnistry of Climate and Environment, Ministry of Foreign Affairs, Ministry of Health and Care Services, Ministry of Trade, Industry and Fisheries, and their relevant directorates.

We appreciate IACG's intention to provide clear and practical recommendations on how to take the global AMR-agenda forward with a strong emphasis on the One Health-perspective, as well as the breadth of the recommendations and the brevity of the report.

The equal emphasis the recommendations place on access on the one hand, and prudent use on the other, is positive and necessary. We also agree with the approach that overuse and misuse of antimicrobials to promote growth and routinely prevent disease in healthy animals and crops, without appropriate indication and the absence of good agricultural practices, needs to be addressed. This is important in order to reduce development of AMR both in animals and humans. Furthermore, antibiotics should only be prescribed by competent, licensed professionals. We also believe it is important to maintain a non-profit policy for prescription, i.e. decoupling of prescriptions and sales of antimicrobial agents in both the human health and the animal health sector and to maintain the prescriber's professional independence.

Prevention of AMR should be strengthened in the recommendations. Infection prevention, including through vaccination, is one central aspect. Adding a recommendation on the need for investing in improved systems for bio-security/sanitation/water/hygiene, is another. Reducing the incidence of infection, which is one of the five strategic objectives in GAP, will reduce the need for antimicrobial agents and subsequently the development of AMR. This recommendation should ideally also include proposals on how to fund activities at country level.

Funding development of new antibiotics is a major priority. Furthermore, we suggest adding a more explicit call for strengthening of funding in other areas than research on drugs and diagnostics, which could also contribute to reducing AMR.

While we fully support the notion that AMR needs increased investments, financing and developing institutions need a clear understanding of context related to the bigger set of health challenges in a country, when assessing potential investments.

We strongly support the aim of strengthening accountability and global governance for AMR. However, we do not see recommendations E1 on establishment of a Global Leadership Group and E2 on an Independent Panel as the preferred way forward to achieving this goal.

The proposed functions for the Group and the Panel raises several questions in relation to existing mandates for the Tripartite Plus organizations. And we see real challenges in securing the legitimacy of a leadership group that inter alia will "set targets" and "identify priorities for R&D", including in the selection of its members. We believe that any governance arrangement for strengthening AMR at global level need to have Member States as the basis. If such a leadership group were to convene a multi-stakeholder partnership platform, we will end up with a governance arrangement lacking both legitimacy and the ability to bring real progress to work at country level.

As regards the recommendation for an Independent Panel, we see also here major challenges regarding the selection of experts and hence the legitimacy of the advice the Panel will publish. We understand that data presented to the panel for its consideration in any case will need to come from the Tripartite Plus-organizations and note that these organisations already have their respective mandates in this area. We furthermore note that the recommendations are silent on such important aspects as who will establish the Group and the Panel, reporting lines and how to secure sustainable funding for their work.

We strongly believe that scaling up efforts through already existing platforms and processes represents the best way in order to take this agenda forward. The draft recommendations should emphasize and explore this even more. We believe that recommendation E 3 provides a good direction; strengthen AMR work through existing organizations and mandates, and on the basis of the MoU signed by the relevant organizations. An alternative to the establishment of a global leadership group to continue to perform the global advocacy-function could be explore the possibility of prolonging the existing mandate of the IACG.

See annex below for additional comments in more detail to the different recommendations.

ANNEX

Comments on the different recommendations in more detail;

Recommendations in A:

- It is good to see that the IACG strongly emphasises equitable access. However, for many of the recommendations listed, it remains unclear how activities at the country level can be funded and implemented. This runs somewhat counter to the report's ambition to produce recommendations that are "practical and feasible".
- We commend that this recommendation is grounded in the importance of clean water, sanitation and hygiene, but wonder why this is not contained in the recommendation itself? Ramanan Laxminarayan has aptly emphasized that antibiotics have been doing the "heavy lifting" in place of clean water, sanitation and hygiene. Investing in these areas will have dramatic results in lowering infection rates, including those that are resistant. We believe that this should be a recommendation on its own, given its vital importance.
- In the consideration section for A 1 there is a call for "establishing (national or regional) antimicrobial production facilities". This seems like a far-reaching first step to mitigating shortages when other less costly solutions have not yet been tested, e.g., paying higher prices or insurance top-up payments, assisting producers to bring their dossiers up to regulatory standards so that they can increase their market sizes, and/or improving susceptibility testing to include older antibiotics. It would be good if the discussion of the WHO meeting on Antibiotic Shortages (December 10-11, 2018 in Oslo, Norway) was reflected in the report.
- Consideration 2E calls for "pooled procurement mechanisms". Whereas pooled procurement has been useful to purchase patented antiretrovirals, there is significant concern that the implementation of large pooled procurement mechanisms may actually worsen the availability of older antibiotics. Many of these antibiotics are being provided under old dossiers that do not comply with current regulations. There is likely only a handful of companies that could comply with a regional pooled procurement tender, which would contribute to further consolidations of the market. It would be good if the discussion of the WHO meeting on Antibiotic Shortages (December 10-11, 2018 in Oslo, Norway) was reflected in the report.
- For recommendation A3 it will be important to ensure that phasing out of antibiotics for growth promotion is not compensated for by an increase in prophylactic or metaphylactic use. This will require robust monitoring systems for total antibiotic consumption to ensure that an overall decrease of antibiotic use in farming is achieved
- While IPC is named in several places, we believe that its function is of paramount importance to reducing the burden of infectious disease for both, resistant and susceptible organisms. We would therefore encourage the IPC to strengthen the commitments to IPC

Recommendations in B;

The development of new antibiotics is obviously a major priority. However,

- it would be good to see a more explicit call for a strengthening of funding in other areas than research on drugs and diagnostics. This could include better surveillance instruments, the development of predictive tools that can assess the likely effect of different policy measures ex ante, and a greater focus on risk communication and behavioural science. These areas will be important for measuring changes over time, identifying the most cost-effective interventions, and ensuring their proper implementation. It would therefore be good to see them placed more prominently than in the current report.
- This is a call for more funding for innovation, which is necessary across all types of microbes and technologies. Yet this recommendation ties the increased investment to Product Development Partnerships (PDPs). PDPs contribute significantly to innovation for neglected diseases, where the market does not function at all. This is evidenced by the static investment in R&D at about USD 3 to 3.5 billion per year. But antibiotics, vaccines, and diagnostics are not complete market failures. The private sector invests significant amounts into each of these areas. The AMR Industry Alliance states that the private sector invested USD 2 billion in antibiotic innovation in 2016. Pfizer has been investing in developing an S. aureus vaccine, which unfortunately failed due to scientific reasons. The first consideration under this recommendation states that "the unclear market potential for antibiotics, diagnostics, and vaccines discourages innovation..." There is a clear market potential for vaccines as evidenced by the strong sales of the pneumococcal and rotavirus vaccines. There is also a strong market potential for diagnostics. The difficulty lies in that diagnostics are more expensive than effective, generic antibiotics. Creating PDPs will not solve these problems, and it crowds out private investment. We need to stimulate greater private investment by creating better incentives and regulations.
- We fully agree that antimicrobials, diagnostics, vaccines, and other technologies need to be affordable and accessible to all who need them. Yet recommendation B2 does not include national government responsibilities to ensuring access. Most existing antibiotics are inexpensive, for example, amoxicillin costs about USD 0.50 per treatment course. They are not priced out-of-reach of national health budgets. Please see the work of the UN Commission on Life-Saving Commodities for Women and Children for concrete actions to make these inexpensive commodities more accessible. Integrating more expensive products in the global access initiatives may be appropriate, but it is also important to stress the role of Universal Health Coverage (UHC) and its role in improving access to these inexpensive commodities
- We agree that existing mechanisms like GAVI, GFATM, UNITAID and CEPI have an important role to play in relation to AMR, including on access to quality antibiotics and vaccines, and that a One Health-perspective need to be applied when decisions on future investments are taken. Initiatives like the Global Fund and UNITAID are already engaged in the AMR agenda in relation to AMR in parasites (malaria), virus (HIV) and in TB; the part of the AMR agenda especially engaging low- and middle income countries. We note that when introducing new vaccines, GAVI is considering

- to not only emphasize their effect on mortality reduction but also whether a vaccine can help reduce AMR.
- Different organizations are already performing significant mapping exercises of R&D efforts, including Pew Charitable Trusts and the AMR R&D Hub. These initiatives should be noted.

Recommendations in C

Regarding recommendation C2 and also D2; we recognize the role of the private sector in fighting AMR. Such engagement could however also raise issues with regards to conflict of interest, including from pharmaceutical companies selling and distributing antibiotics. Such conflicts of interest need to be acknowledged, and proper controls put in place.

Recommendations in D

The IACG rightly points out the need for more funding for AMR. However,

- it would be important to state clearly that the funding needed must not be diverted from existing health initiatives in LMICs, but needs to be additional funding while AMR is of high importance to health, it is by no means the only important area. It should also be noted that some of the funding mechanisms the report mentions (JPI sAMR, Fleming Fund) focus primarily on the development of diagnostics and new drugs. Additional funding is also urgently needed for infection prevention and control, surveillance, education and the establishment of universal health coverage, in the absence of which new drugs could not be utilised appropriately.
- financing and developing institutions need to have a clear understanding of context
 when they assess potential investments. Countries face a range of challenges,
 including climate change, poverty, and capacity-building. Some countries may be only
 marginally impacted by AMR. It is important that the country's context is the focus of
 investment decisions.

Comments from Peruvian Institutions on Draft of Recommendations of IACG on Antimicrobial Resistance

The draft of the IACG recommendations about antimicrobial resistance was shared with the Ministry of Health (MINSA), Ministry of Agriculture (MINAGRI) and Ministry of Production (PRODUCE) of Peru. These three entities derived the analysis of the document to their respective technical areas.

These are the comments and suggestions of the three sectors involved in the response to antimicrobial resistance in Peru: human health represented by "Instituto Nacional de Salud" (INS – MINSA), animal health represented by "Servicio Nacional de Sanidad Agraria" (SENASA – MINAGRI), and productive sector represented by "Sanidad Pesquera" (SANIPES – PRODUCE).

Human Health - Instituto Nacional de Salud (INS):

Comment: The success of the gradual implementation of the "ONE HEALTH" approach in response to the antimicrobial resistance requires the active and joint participation of all the stakeholders from the human, animal and environmental sectors. The tripartite mechanism (WHO, FAO and OIE) is an important but incomplete effort, although the official incorporation of UNEP by the end of 2018 corrected this situation. This positive joint work at the global level also merits action at the country level, which requires a greater involvement of the national institutions responsible of the environment. To accomplish this goal, it is needed the sensitization of the national stakeholders on environment about the negative consequences of the dissemination of the antimicrobial resistance on human and animal health. It also requires a more research at the national level about the status of the antimicrobial resistance and the role of the environment at the national level, especially in low-resource settings.

Suggestion: Consider include in Recommendation E3 (page 16) that the activities integrated under the approach "ONE HEALTH" require additional efforts to involve those responsible at the national level of the environment, given the recent inclusion of PNUE and the scarce evidence and regulations about antimicrobials and antimicrobial resistance in the environment at low-income countries.

2. Animal Health – Servicio Nacional de Sanidad Agraria (SENASA):

Suggestions:

Recommendation A1

- a. It must be stated that antimicrobial prescriptions should be prescribed exclusively by competent professionals.
- b. The use of antimicrobials as probiotics en the formulation of animal feed should be prohibited.

Recommendation A2

c. Deadlines should be established for the approval of the national plans in order to achieve the SDGs.

Recommendation A3

d. A schedule must be set for compliance with this recommendation.

Recommendation B3

- e. Establish a network of Reference Laboratories on AMR topics.
- f. Encourage the development of new analytical tests for AMR

3. Productive Sector – Sanidad Pesquera (SANIPES):

Suggestions:

- a. Please, consider include the references that support the information of the first paragraph (page 2).
- Please, in the second paragraph on page 2, consider include the reference to this document in line 12: Antimicrobial resistance: Invest in innovation and research, and boost R&D and access. IACG discussion paper, June 2018.

Recommendation A1

- c. On page 3, under the section "Considerations for this recommendation (A1)", line 3, consider include (in red color): "The IACG recognizes that effective systems for infection prevention and control, including vaccination, clean water, sanitation and hygiene, as well as Good Management Practices, biosecurity and good animal welfare in farming and other phases of the food chain, avert infections in health care and farm settings."
- d. On page 5, under the section "Considerations for this recommendation (A1)", line 1, consider include (in red color): "The IACG emphasizes that there is an urgent need to strengthen national integrated transectorial surveillance and regulatory frameworks and enforcement capacity in all countries to support effective national responses to antimicrobial resistance..."

Recommendation A2

e. On page 5, under the section "Considerations for this recommendation (A2)", fourth bullet, consider include (in red color): "Understanding the global impact and free dissemination along borders of AMR, the IACG further recognizes that cooperation and solidarity are required among all countries for an effective global response and to ensure that adequate financial and technical resources are available to support implementation of national action plans, based on the international agreements of international cooperation for development, including in low- and middle-income countries."

Recommendation B3

f. On page 9, under the section "Recommendation B3", consider include a new bullet: (in red color): "Promoting the development of analytical skills which will be adequate and

- standardized to provide support to the research, surveillance and monitoring activities."
- g. On page 9, under the section "Recommendation B3", consider include in bullet d: (in red color): "Promoting openness and transparency in data from all research and monitoring and surveillance sources. The report of the results from the research, surveillance and monitoring activities should be adequate and available to the public."

Recommendation C2

- h. On page 11, under the section "Recommendation C2", consider include a new bullet: (in red color): "Development of policies for the promotion of private investments in research and development on antimicrobial resistance."
- i. On page 11, under the section "Recommendation C2", consider include a new bullet: (in red color): "Contributions to sensitize and provide information to the end-users of their products."

Recommendation D2

j. On page 13, under the section "Recommendation D2", consider mentioning that these actions are aligned with the Sustainable Development Goals 2030.

Singapore

From: <u>Lin Yueh Nuo (NCID)</u>
To: <u>IACG-secretariat</u>

Cc: Ching Ying KONG (MOH; Geraldine CHENG (MOH; Melody TAY (MOH); Audrey CHEN (AVA; Kelvin LIM (AVA); Lee

Tau Hong (TTSH); Astrid Khoo Pheng Pheng (NCID); Keefe CHIN (MFA; Jeffery CUTTER (MOH

Subject: Singapore"s comments on Draft IACG Recommendations

Date: Tuesday, February 19, 2019 05:55:35

Attachments:

IACG Secretariat,

Firstly, we would like to thank the IACG for the work done in drafting these recommendations.

Singapore has no objection to these recommendations in general, and welcomes the increasing involvement of the United Nations Environment Programme (UNEP).

On some of the terms used, we suggest greater clarity on the scope of "waste management" is needed. "Pharmaceutical waste" is mentioned on page 3, while in other pages, such as recommendations A1, A2, B1, B2 and C2, the term "waste management" is not well defined. It would be useful to keep it consistent and improve the clarity.

We also propose a slight amendment to the wording of recommendation A3, to specifically identify CIAs as those listed by WHO and to use common terminology. The proposed change and more specific comments are found in the attached document, for IACG's consideration.

Thank you.

Best Regards, Yueh Nuo

Lin Yueh Nuo (Ms)

Deputy Director, Antimicrobial Resistance Coordinating Office (AMRCO)

NATIONAL CENTRE FOR INFECTIOUS DISEASES, Ministry of Health Singapore

SINGAPORE'S COMMENTS ON DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE, 19 Feb 2019

General comments

- 1. Singapore has no objection to the recommendations in general, and welcomes the increasing involvement of the United Nations Environment Programme (UNEP).
- 2. In general, greater clarity on the scope of "waste management" is needed. "Pharmaceutical waste" is mentioned on page 3, while in other pages, such as recommendations A1, A2, B1, B2 and C2, the term "waste management" is not well defined. It would be useful to keep it consistent and improve the clarity.

Specific comments

A. ACCELERATE PROGRESS IN COUNTRIES

Recommendation		Singapore's comments:
A1	The IACG calls on all Member States to ensure equitable and affordable access	No objection to this recommendation.
	to existing and new quality-assured antimicrobials and their prudent use by	
	competent, licensed professionals* across human, animal and plant health.	However, it should be noted that ensuring
		affordable access while operating on a free-
	This recommendation must be supported by efforts both to reduce the need for	market access model may pose a challenge
	antimicrobials and improve access through:	to some countries, particularly in the animal
	a. Lowering the prevalence of infection through clean water, sanitation and hygiene;	sector.
	b. Decreasing the likelihood of diseases and their spread through delivery of existing	(b) Delivery of versions and IDC massages
	vaccines and strengthening infection prevention and control measures;	(b): Delivery of vaccines and IPC measures
	c. Ensuring best practices in terrestrial and aquatic animal and plant health, food production and waste management;	should be complemented by education strategies, in particular those that debunk
	d. Supporting behaviour change through effective communication and incentives	anti-vaccine groups and the associated false
	targeted at the public and professionals in human, terrestrial and aquatic animal and	information.
	plant health, as well as food production and the environment;	miormason.
	e. Developing national instruments based on international standards for equitable	(d): Messaging needs to be at the
	access to and prudent use of existing and new quality-assured antimicrobials in	appropriate level of the target group, and
		should consider the existing knowledge

humans, animals, plants and food production, as well as waste and water management in health care, manufacturing and farming-related activities; and f. Strengthening national surveillance, regulatory and accountability mechanisms.

* The IACG recognizes that in settings where trained prescribers are in short supply, non-physicians (such as nurses, paramedics and community health workers) and veterinary paraprofessionals may also be trained and authorized to prescribe or administer some antimicrobial agents.

gaps. Narratives will also need to be integrated, for instance, before delving into the message of AMR and prudent use of AM, there may be fundamental gaps in knowledge on what bacteria/viruses are, what antibiotics do, why and when we need/do not need them etc. Therefore, there needs to be stringing of messages in a coherent manner, while avoiding messaging fatigue. While countries should have oversight of the priority areas to educate on, there should be synchronisation of messaging across sectors. A consistent narrative could be encouraged.

Under "Considerations for this recommendation:"

Pg 4. On "Establishing antimicrobial production facilities: Some governments or regional entities may consider establishing production facilities or contracting manufacturers to help mitigate shortages and ensure a resilient supply of antimicrobials, particularly antibiotics and vaccines for human and animal health, paying due consideration to manufacturing standards and quality assurance for health commodities."

- (i) To include considerations on "Facilitating supply chains to antimicrobial production facilities". This is a form of Public-Private Partnership. Aside from establishing antimicrobial production facilities, strong logistics and supply chain links are equally important to support antimicrobial access. Commercial interests (e.g. strong demands) and regulatory areas (such as registration) are also considerations of the private sector.
- (ii) To provide more clarity on what these "health commodities" are.
- (iii) Propose removing "environmental health sectors" (in the first line) as that
- Pg 4. On "The prudent use of antimicrobials across the human, animal, plant and environmental health sectors requires appropriate attention to and investment in

	training, accreditation and regulation of professionals, including physicians, pharmacists, veterinarians and other specialists across human, terrestrial and aquatic animal and plant health, as well as in food production and the environment."	was not included on page 3. Prudent use is not applicable to environmental health sectors.
	Pg 5. "The IACG emphasizes that there is an urgent need to strengthen national surveillance and regulatory frameworks and enforcement capacity in all countries to support effective national responses to antimicrobial resistance, including on the prudent use of antimicrobials and their sale, particularly over-the-counter and on the internet, as well as sound environmental and waste management practices. Surveillance systems should include a set of specific indicators to enable monitoring of access, availability and affordability of antimicrobials and related commodities."	(iv) Singapore recognises the problem of internet sales, but would like to highlight that internet sales are not easily controlled, particularly purchases from platforms outside of a country's jurisdiction. Therefore, a concerted effort (bilateral, multilateral) is needed to detect and remove avenues for such purchases.
A2	The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs that, at a minimum, include: a. Prioritized actions and interventions that are specific to the national context and that are costed and funded, including with adequate domestic resource allocations; b. Strengthening key national systems for infection prevention, monitoring, integrated surveillance, procurement of health commodities and waste management; c. Technical co-operation, capacity development, research and advocacy components, including support for champions at national and local levels to mobilize action on antimicrobial resistance; and d. Effective national coordination, accountability and governance mechanisms.	No objection to this recommendation
A3	The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion , consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins).	Singapore proposes to re-word this recommendation as follows: "The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and

WHO), starting with an immediate end to the
use of <u>antibiotics categorised as highest</u>
priority critically important in WHO's list of
Critically Important Antimicrobials for Human
Medicine (i.e. quinolones, third- and higher-
generation cephalosporins, macrolides and
ketolides, glycopeptides and polymyxins).
D ()
Rationale:
(i) To adopt the common terms, "antimicrobials" instead of "antibiotic
agents", in making reference to the WHO
List of CIAs, for consistency;
List of OlAs, for consistency,
(ii) To state clearly the antibiotics are
categorised as "highest priority critically
important" in WHO's List of Critically
Important Antimicrobials for Human
Medicine. This will provide better clarity.

B. INNOVATE TO SECURE THE FUTURE

Recom	mendation	Singapore'
B1	The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials - particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials - for human, terrestrial and aquatic animal and plant health through: a. Financial and non-financial incentives strategically targeting the most important research and development needs, scientific challenges, and market barriers based	No objection to this recommendation.

	on the principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance; and b. Building upon existing Product Development Partnerships in human health and establishing more of them, particularly for terrestrial and aquatic animal and plant health.	
	Under "Considerations for this recommendation":	
	Pg 8 "The IACG underlines that additional funding combined with financial and non-financial incentives is particularly required to bring innovative products from fundamental research to registration and implementation, including to accelerate clinical trials in humans and experimental work in animals and plants, and to enhance the role of small and medium enterprises in research and development."	Clinical trials should also extend to animals. One of the issues faced is that there are insufficient clinical trials/ work for new antimicrobials for use in animals.
B2	The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.	No objection to this recommendation.
B3	The IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context by: a. Undertaking coordinated global mapping of research and development activities and funding to address antimicrobial resistance; b. Establishing and maintaining a platform for sharing information on research and compounds in development in both ongoing and completed research and development activities; c. Promoting synergies and opportunities for collaboration among funders and researchers in human, animal and plant health, and the environment; and d. Promoting openness and transparency in data from all research and monitoring and surveillance sources.	No objection to this recommendation. However, more clarity is needed on who is to undertake the coordination of "global mapping of RnD initiatives" and establishment of a "global platform for sharing information". This recommendation seems to have left it to the "existing RnD platforms to formalise information sharing and collaboration arrangements. Albeit challenging, what is needed is higher level coordination perhaps at the Tripartite agencies level.

	(d) Singapore agrees with the need for transparency and information sharing, however there might also be practical concerns of researchers and private entities (businesses etc.), such as, the protection of intellectual property, especially with non-publicly funded research.
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C. COLLABORATE FOR MORE EFFECTIVE ACTION

Recom	mendation	Singapore's comments
C1	The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels through:	No objection to this recommendation. However, public education should also be included. Apart from engaging the civil
	 a. Strengthening their roles in accountability, advocacy, monitoring progress and ensuring prudent use of antimicrobials; b. Promoting synergies with consumer and civil society groups active in other sectors, including in climate change and the environment, responses to HIV, TB and malaria, Universal Health Coverage and other aspects of the SDGs; and c. Provision of political, financial and technical support for civil society organizations to enhance their engagement, including for work with governments. 	society and the private sector, public and school education on AMR should be included for their wide-ranging impact. If we deemed AMR to be an issue as serious as climate change, HIV, TB, malaria, there should be more direct public education on this.
C2	The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels in order to ensure: a. Affordable access, prudent use and stewardship of antimicrobials; b. Ethical production, distribution and marketing practices, including through environmentally sustainable production and waste management and the elimination of inappropriate incentives to sell antimicrobials; c. Engagement by the private sector in collaborative efforts to collect, analyze and use data and realign economic incentives to improve production, distribution and marketing practices; and d. Contributions to addressing antimicrobial resistance through testing of innovative approaches, corporate social responsibility, and similar initiatives.	No objection to this recommendation.

D. INVEST FOR A SUSTAINABLE RESPONSE

Recon	nmendation	Comments
D1	The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and One Health "lens" when making investments through: a. Official Development Assistance; b. South-South cooperation; c. The International Development Association (IDA) replenishment process from IDA19 onwards; d. Financial support, grants, loans, credits and insurance for terrestrial and aquatic animals and plants, health, development, food systems, manufacturing of health products, the environment and other relevant areas.	No objection to this recommendation. To consider a better alternative term for "lens" for the purpose of an international document. A more defined term would leave less room for interpretation.
D2	The IACG emphasizes the need for increased investment in the global response to antimicrobial resistance. It urges existing and future financing mechanisms in human, animal and plant health, as well as food production and the environment - including Gavi – the Vaccine Alliance, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Global Financing Facility, Multilateral Climate Funds, Unitaid, as well as future financing streams for Universal Health Coverage and other priority development issues, and their donors - to give antimicrobial resistance greater priority in their resource allocations. It further calls upon public, private and philanthropic donors in human, animal and plant health, as well as food production and the environment, to increase funding to contribute to addressing antimicrobial resistance, including to support implementation of National Antimicrobial Resistance Action Plans.	No objection to this recommendation.

E. STRENGTHEN ACCOUNTABILITY AND GLOBAL GOVERNANCE

Recommendation	Singapore's comments
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E1	The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat, to: a. Maintain urgency, public support, political momentum and visibility of the antimicrobial resistance challenge on the global agenda, and set targets; b. Advocate for action, including support for the expanding work of the Tripartite agencies (FAO, OIE and WHO), UN Environment (UNEP) and other international and regional entities; c. Monitor and report on progress, gaps and accountability in the global response to antimicrobial resistance; d. Expand multi-stakeholder engagement by establishing a partnership platform with the participation of Member States, UN agencies, international and intergovernmental organisations and regional entities, civil society, the private sector, researchers and other key stakeholders to develop and work towards a shared global vision and coordinated action on antimicrobial resistance; e. Provide advice and guidance on reports of the Independent Panel on Evidence for Action against Antimicrobial Resistance (recommendation E2); f. Monitor and advocate for the inclusion of antimicrobial resistance and a One Health "lens" in investments and programmes of major financing instruments for agriculture, health, development, food production and other relevant areas (recommendation D1); g. Identify priorities for research and development and facilitate implementation research in a One Health context; and h. Define the financial needs and gaps for the global response to antimicrobial resistance, including the costs of inaction and anticipated returns on investment.	No objection to this recommendation.
E2	The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.	No objection to this recommendation.
E3	The IACG requests the Tripartite agencies (FAO, OIE and WHO) together with UNEP and other UN agencies, in the context of UN reform, to further strengthen joint One Health action, based on country priorities and needs, by	No objection to this recommendation.

	onhancing their erganizational canacity and providing adequate and sustainable core	
	enhancing their organizational capacity and providing adequate and sustainable core funding for antimicrobial resistance-related activities in order to:	
	a. Integrate antimicrobial resistance-related activities into country UN Development	
	Assistance Frameworks;	
	b. Provide and update effective normative guidance, standards and tools when	
	needed;	
	c. Advise on priority evidence-based interventions and actions;	
	d. Provide coordinated technical co-operation and capacity building, including One	
	Health regional platforms for technical co-operation; and	
	e. Guide, support, monitor and evaluate implementation, including on infection	
	prevention, integrated surveillance, data quality and harmonization, risk assessment,	
	and demand forecasting and supply management.	
E4	The IACG recognizes the ongoing process led by Member States to develop the	No objection to this recommendation.
	Global Development and Stewardship Framework to Combat Antimicrobial	
	Resistance and urges the Tripartite agencies (FAO, OIE and WHO) and UNEP	
	to expedite its development in line with the scope described in the 2015 World	
	Health Assembly resolution on antimicrobial resistance (WHA68.7). As Member	
	States finalize this process, they should also consider the need for new international	
	instruments.	

Spain

After receiving the communication sent by the Spanish Embassy in Geneva about the request for comments on the draft recommendations for the international response to antimicrobial resistance, presented by the Inter-Agency Coordination Task Force on Antimicrobial Resistance (IACG), The National Plan against Antibiotic Resistance (PRAN) coordinated by the Spanish Agency of Medicines and Medical Devices (AEMPS) informs of the reception of comments by the Embassy in Geneva and then details the comments made by the PRAN Coordination Unit.

DOCUMENT:

DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE (For public discussion prior to finalization)
January 2019

DATE OF COMMENTS:

January, 18th 2019

COMMENTS:

PART A: Accelerate Progress in Countries:

- <u>Recommendation A1</u>. The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health.
 - As a control measure, the indications of the new antimicrobials could be more restricted.
 - In this context, Spain is working to promote the implementation of the Programs for the Optimization of the Use of Antibiotics (PROA) both in Hospital and Community sector.
 - Also Spain is working in the Programs for the reduction and prudent use of antibiotics in the different sectors of animal production that are also being developed in Spain as a model of success in the prudent use of antibiotics extrapolated to the rest of the Member States of the U.E.
- <u>Recommendation A2</u>. The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs.
 - PRAN agrees with this recommendation, it is important to develop and implement strategies at the national level to fight against resistance to antibiotics, as well as one health strategies in interprofessional cooperation at the national level and international cooperation.

- <u>Recomendación A3.</u> The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins)
 - In Spain, the use of antibiotics as growth promoters has been forbidden since January 1, 2006, in accordance with with Regulation (CE) No. 1831/2003 of the European Parliament and the Council of September 22th 2003 on additives in animal feed.
 - The PRAN emphasizes the importance of this prohibition as well as the elimination of the use of antibiotics as a prophylactic treatment.
 - Antibiotics categorized as of highest priority critically important, should be used in animals as a last resort with a prior diagnosis that justifies such use and with a sensitivity test that indicates the use of such antibiotics as the only option to preserve the animal's health.

PART B Innovate to secure the Future:

- <u>Recommendation B1</u>. The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials - particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials - for human, terrestrial and aquatic animal and plant health.
 - o PRAN agrees with this recommendation
 - In the case of Spain, it is necessary to obtain financing through our National Health System.
- <u>Recommendation</u> n B2. The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.
 - o PRAN agrees with this recommendation
- <u>Recommendation</u> B3. The IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context.
 - o PRAN agrees with this recommendation

- Spain actively supported the launch of the G-20-Hub AMR Global R
 D during an event that Germany organized at the World Health Assembly (21-26 May 2018, Geneva).
- O About research and development for both prevention and diagnosis and for new antimicrobial therapies, it is worth noting that the Spanish Action Plan on AMR works together with the Carlos III Health Institute (the main public research entity financing, managing and carrying out biomedical research in Spain) as Spanish representatives in the Joint Programming Initiative on Antimicrobial Resistance (JPI-AMR).
- In addition, Spain participates in the European Joint Action on Antimicrobial Resistance and Infections associated with healthcare (EU-JAMRAI) as leader of three workpackages (WP2 "Dissemination", WP8 "Awareness and communication" and WP7 "Appropriate use of antimicrobials in humans and animals").
- Encouraging research and development of better technologies for prevention, diagnosis and new antimicrobials requires mainly 1) consistent and appropriate investment and funding to favor the development of new molecules and 2) a very significant effort to promote cooperation strategies. Cooperation and networking are already being developed within the framework of different global R & D strategies. However, the initiatives are multiple and common platforms and their promotion are needed to channel these efforts and make them more effective.

PART C Collaborate for more effective actions:

- <u>Recommendation C1</u>. The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels.
 - o PRAN agrees with this recommendation.
- <u>Recommendation C2</u>. The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local.
 - o PRAN agrees with this recommendation
 - The "One Health" approach in the strategies against antibiotic resistance must be essential, as well as the cooperation between all the areas and responsibles involved. Work must be done with regional governments to strengthen outbreak surveillance and

- reporting, harmonize the systems of surveillance and control of infections associated with health care, and reinforce them so that multidisciplinary teams can increase their ability to react to alerts.
- o Regarding the private sector, it is important that they become involved and aware of the great global of antibiotic resistance.
- It is considered necessary to cooperate to develop AMR surveillance capabilities by establishing or adopting quantitative indicators of consumption of common antibiotics already approved that should be part of a mandatory strategy. This global and mandatory system could lead to better control of the AMR situation.

PART D Invest for a Sustainable Response:

- <u>Recommendation D1</u>. The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and One Health "lens" when making investments.
 - We believe that this recommendation could be complicated to carry out globally.
- Recommendation D2: The IACG emphasizes the need for increased investment in the global response to antimicrobial resistance. It urges existing and future financing mechanisms in human, animal and plant health, as well as food production and the environment including Gavi the Vaccine Alliance, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Global Financing Facility, Multilateral Climate Funds, Unitaid, as well as future financing streams for Universal Health Coverage and other priority development issues, and their donors to give antimicrobial resistance greater priority in their resource allocations. It further calls upon public, private and philanthropic donors in human, animal and plant health, as well as food production and the environment, to increase funding to contribute to addressing antimicrobial resistance, including to support implementation of National Antimicrobial Resistance Action Plans.
 - This should be a recommendation of high priority at a global level, with the involvement of the most relevant organizations in the matter.
 - Cooperation and networking are already being developed within the framework of different global R & D strategies. However, the initiatives are multiple and common platforms and their promotion are needed to channel these efforts and make them more effective.

PART E Strengthening Accountability and Global Governance:

- <u>Recommendation E1:</u> The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat.
 - At this point it is important to take into account the idiosyncrasy of each country
- <u>Recommendation E2:</u> The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.
 - It is always very positive to know the experience of other countries because it helps to improve and advance.
- Recommendation E3: The IACG requests the Tripartite agencies (FAO, OIE and WHO) together with UNEP and other UN agencies, in the context of UN reform, to further strengthen joint One Health action, based on country priorities and needs, by enhancing their organizational capacity and providing adequate and sustainable core funding for antimicrobial resistance-related activities
 - O It is necessary to promote the "One Health" approach in all the strategies against antibiotics resistance that are carried out in the Member States and in the rest of the countries, on the other hand it needs consistent and adequate investment and financing to favor the development of "One Health" initiatives as well as promotion of the strategies that are already implemented.



Memorandum

19 February 2019

Ministry of Health and Social Affairs

Comments on the Ad hoc Interagency Coordination Group's draft recommendations on antimicrobial resistance

This memorandum has been written to provide feedback on the draft recommendations of the ad hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance (AMR). Relevant sectors have been involved in the preparation of this response.

General comments

Sweden finds the recommendations well written and agrees with the main points raised including the need for a shared global vision, narrative and targets. As expressed in previous communication, it is of great importance that the follow-up of the high-level meeting on AMR in the UN General Assembly boosts coordination and commitments for national implementation across the UN-system and beyond, and as per the One Health principle. Furthermore, Sweden appreciates that clear links are being made to the importance of AMR for fulfilment of the UN Sustainable Development Goals (SDG).

Sweden believes that the recommendations are comprehensive and relevant, although we would have liked them to go further and be more concrete and output oriented. It should be recognized that countries have different situations and starting-points but still, more imperative language can be used.

Although countries may have to use different and step wise approaches, it should be clearly stated that:

- antibiotics should not be given without a proper diagnosis, and antibiotics should have the status of prescription only medicines. This highlights the importance of health systems strengthening and of access, not only to antibiotics, but also to diagnostic tools.
- antibiotics should not be used in plant health.
- antibiotics should not be used for growth promotion in animals and must therefore be phased out.
- the use in aquatic animals leading to direct emissions in the environment should be restricted.
- pollution control measures should be practiced both in production and in waste management.

Sweden believes that strengthened global leadership in line with the recommendations of the One Health Global Leadership Group and the Independent Panel on Evidence for Action AMR is needed. We want to emphasize the importance of Tripartite Plus having a central role in the global accountability and governance system and Sweden supports the recommendation to further strengthen the Tripartite Plus joint One Health action. It is of the utmost importance that the members of the Tripartite Plus now acts forcefully to help drive this issue forward globally.

A. Accelerate progress in countries

Sweden appreciates that this is the very first recommendation as it is the most important one. Without building and sustaining effective and tailored national responses, there will be no success in containing AMR. National commitments with sufficient and sustainable funding is key. Sweden appreciates the attention given to prevention and to access and stewardship of antibiotics and would also like to highlight the importance of access to diagnostic tools.

Prudent use of antimicrobials is important, both in the human sector and for animal health, as overuse and misuse of antibiotics in all sectors contributes to the problem of resistance. In section A there is mentioning of prudent use across the human, animal, plant and environmental health sectors without further explanations of what this means in the different sectors. Without clear definitions and targets of what signifies prudent use in the different sectors, this recommendation risk being ineffective.

It is an important signal that inappropriate use of antimicrobials, such as the use for growth promotion, should be avoided and to establish that

eliminating the use of Highest Priority Critically Important Antibiotic Agents is only a first step. However, supportive measures, such as advice about feed, care and infection control should be used in the phase-out process to avoid setbacks. It is important to recognize that it is possible to combine sustainable and economically viable livestock production with a low antibiotic use. Countries should be encouraged to engage with all stakeholders in promoting the prudent and responsible use of these important medicines, including across the agricultural sectors

Sweden appreciates the focus given to surveillance and monitoring, and would suggest an even stronger language on promotion of surveillance and sharing of data in all sectors and especially in animals. There is an urgent need to further develop and establish a One Health monitoring capacity, despite the challenges, including technical and legal issues such as data protection for example in the EU (GDPR). These recommendations could be strengthened even further and it is important to more clearly promote harmonization of the surveillance. The statement; "To the extent possible, they should also provide harmonized or equivalent data (...)" could be expressed in a stronger language. The opportunity of benefitting from investments made in disease preparedness and prevention as part of IHR should be highlighted more. This includes surveillance both on the animal and human side, lab capacity etc.

On the same note, measurable targets and core indicators are mentioned but deserve more attention. Experience shows that monitoring and transparent reporting of progress towards set targets have a significant impact on incentives for mobilizing action.

B. Innovate to secure the future

Sweden agrees that investment in new antimicrobials - particularly antibiotics, as well as diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials is urgently needed. Sweden wishes to emphasise that market failure of antibiotics calls for new and innovative incentives and business models. The present situation is not good enough. Although the IACG recognizes the need to develop and provide financial and non-financial market incentives for research and development to address antimicrobial resistance, we lack new and concrete recommendations on how to accelerate innovation in practice.

Sweden agrees that more funding is required for implementation and operational research, including on mechanisms of transmission of drug resistant infections, implementation of effective approaches, behaviour change, communication, infection prevention, prudent use of antimicrobials and effective soil, water and waste management. Although there might be need for further development, we would like to point out that there are tools for soil, water and waste management available already. Attention should also be given to the implementation of these. There is also a need for research on human perceptions, beliefs and social relations that influence the human behaviours that spur the expansion of AMR.

Sweden supports that the IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts. In relation to this we appreciate the recognition and support for the JPIAMR and its activities throughout the document.

C. Collaborate for more effective action

Sweden acknowledges the importance of this recommendation. A number of groups are being mentioned in the texts and we would like to further emphasize the important roles that farmers, consumers and the general public (who are occasionally patients) have played in decreasing the use of antibiotics in Sweden. In the recommendation C1(b) sexual and reproductive health and rights (SRHR) should be mentioned, as AMR is of detrimental importance for infant and maternal health, sexually transmitted diseases and unsafe abortions.

The responsibility of the private sector to limit environmental emissions should be highlighted further. Pollution control measures should be guided by the Polluter Pays Principle. Sustainable public procurement plays an important role in demanding an environmentally sustainable production of antimicrobials.

D. Invest for a sustainable response

In all recommendations throughout the report, access to financial resources at national and international levels is decisive although it has not always been spelled out. The statements on applying an AMR lens for investments and allocation of resources from, or in concordance with, existing fund streams are important and well phrased. The metaphor should however be further

concretized by giving examples e.g. "Laboratories that have been built for TB should be used for AMR as well". It should also be acknowledged that specific funding will be needed for certain initiatives that cannot leverage resources within existing funding mechanisms. A guiding mechanism on where to apply funding from might be needed. Solely applying an AMR lens on existing funding might make it less clear from which sources to apply for funding for designated AMR investments. It is also important to improve communication and information flow regarding which funding that has already been made available to systems that can also be used for the AMR response (surveillance, lab capacity, board control etc).

Furthermore, Recommendation D2 emphasizes funds for human health initiatives. We suggest including the Global Environment Facility (environment) and future financing streams for "water, sanitation and hygiene (WASH)".

E. Strengthen Accountability and Global Governance

Sweden agrees that stronger and sustained global leadership, advocacy and a more powerful global narrative and vision are all needed to advance the global response to antimicrobial resistance. We support the recommendation to form a Health Global Leadership Group. At this stage we would however like the recommendation to be less detailed about the composition etc. The form of the group, for example who should be a member, can be established at a later stage. Spelling this out in too much detail at this stage might hamper the decision to form such a group.

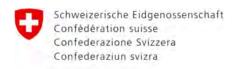
Sweden support the recommendation to form an Independent Expert Panel on Evidence for Action on AMR.

Sweden supports the recommendation to further strengthen the Tripartite Plus joint One Health action. Creating multiple new groups might introduce excessive complexity. The full potential of already existing organisations should be used. The work must be organized and conducted in an efficient and effective manner and it should promote synergies with existing structures and systems. Sweden emphasizes the importance of coordination with the forthcoming framework (A Global Development and Stewardship Framework) to be developed by the Tripartite Plus.

Finally, Sweden would like to emphasize the importance of follow-up and evidence based evaluation of the recommendations. It is crucial to have indicators, statistics and goals to monitor if progress is being made.

Priorities for the UN Secretary General's report

- Accelerate progress in countries. UN endeavours will only provide added value if it drives change and has impact at the local level.
- Cooperation and solidarity are required among all countries to ensure that adequate financial and technical resources are available to support implementation of national action plans in low- and middleincome countries (LMIC).
- AMR must be tackled through a One health approach. Much of the
 antibiotics used in the world today are used in animals. Phasing out
 of growth promotors to animals must continue and, to be successful,
 it must be underpinned by investments in sustainable production
 practices that minimize the need for antimicrobials.
- There is an urgent need to develop new antibiotics.
- A One Health Global Leadership Group should be set up to keep AMR on the global agenda.
- An Independent Panel on Evidence for Action against AMR should be set and should consist of experts.
- The Tripartite Plus should be strengthened and continue to have an important role in the global response to AMR.
- Environmental concerns should be raised and kept on the agenda.
- The report must be prospective and drive change. Concrete action is needed now.



Swiss Confederation

Federal Department of Home Affairs FDHA

Federal Office of Public Health FOPH

Division of International Affairs

Written feedback of Switzerland on the draft IACG recommendations:

General remarks:

- With regard to the human sector (A1, A2, B1, B2, C1), the recommendations are not really new, but they do make sense. To a large extent, we are already implementing these recommendations in our national strategy for Switzerland (FOPH).
- For Switzerland, international collaboration/cooperation really adds value in the field of AMR. Efforts cannot be made only at the national level.
- The One Health Approach, which has been applied across the board and includes a very large sphere of influence, is to be welcomed.

A1:

- Prudent use of antimicrobials being key in preventing antimicrobial resistance, we suggest emphasizing the importance of prudent use by completing the following sentence in the box on page 3 as follows:
 - "This recommendation must be supported by efforts both to reduce the need for antimicrobials, **enhance their prudent use**, and improve access through.... "
- We also suggest completing the following sentence in the box on page 3 as follows:
 "The IACG calls on all Member states to ensure equitable and affordable access to existing
 and new quality-assured antimicrobials as well as alternatives and their prudent use by com petent, licensed professionals across human, animal and plant health."
 N.B. Alternatives would be vaccines, phytomedicines or in agriculture e.g. resistant varieties,
 products with antagonists, etc.

A3:

• Switzerland fully supports recommendation A3 because antimicrobial performance enhancers have been banned since 1999 in Switzerland. Switzerland considers the worldwide stop of growth promoters in animals as a very central issue.

B3a :

- Switzerland suggests some changes in the formulation of *letter a* of recommendation *B3* in order to better take into account / reflect the mission of the Global AMR R&D Hub established by the G20 in May 2018 with the purpose to address challenges and improve coordination and collaboration in global AMR R&D:
 - a."collaborating with and supporting the Global AMR R&D Hub in carrying out its undertaking coordinated global mapping of research and development activities and funding to address antimicrobial resistance."

B3d:

• "Promoting openness and transparency in data from all research and monitoring and surveillance source": It should be noted that data protection provisions set strict limits to full transparency of monitoring and surveillance data depending on the country.

C2:

 Active involvement of the private sector is probably a controversial recommendation for many state actors and still formulated too generally. As far as R&D of new AB is concerned, it is still unclear to state actors where exactly they should target the global R&D mechanisms at national level. With regard to stewardship, it is also questionable whether this should be the role of private actors, as they are following their own interests and therefore are not impartial.

E1:

• The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance in order mainly to maintain urgency, public support, political momentum and visibility of the AMR challenge on the global agenda. This proposal is useful for us if the Tripartite with UNEP cannot take over this role themselves. We see this Leadership Group taking over and further the mission of the IACG in the future.



UK Government response to the UN IACG Public Discussion on: Draft recommendations of the UN Ad-hoc Interagency Coordination Group on Antimicrobial Resistance

February 2019

Title:

UK Government response to the UN IACG Public Discussion: Draft recommendations of the UN Ad-hoc Interagency Coordination Group on Antimicrobial Resistance

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The UK has responded with overarching comments to the IACG's recommendations, and high-level comments for each of the recommendations

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- Foreign and Commonwealth Office (FCO), including:
 - o UK Mission to United Nations, New York
 - o UK Mission to the United Nations, Geneva
- Department for Environment, Food and Rural Affairs (DEFRA)
- Veterinary Medicines Directorate (VMD)

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UK Government Priority Recommendations

Methodology used and overview of UK priorities

- The Government of the United Kingdom and Northern Ireland (the UK Government) thanks the UN Ad Hoc Interagency Coordination Group on Antimicrobial Resistance (the IACG) for its work to develop the draft recommendations and for the opportunity to comment prior to their transmission to the UN Secretary General in March/April 2019.
- Considering the nature of this exercise (i.e. an opportunity for Member States to share their comments rather than a consultation process where the IACG is expected to act on feedback), the UK Government has chosen to focus on the recommendations that we consider to be the highest priority for the international community.
- 3. These priority recommendations were selected using the following criteria:
 - Recommendations that address a gap in the current global response to AMR;
 - Recommendations that are not getting traction in other fora or other mechanisms;
 - Recommendations that can be implemented by Member States and UN agencies.
- 4. On this basis, the UK considers the following recommendations as the highest priority¹:
 - IACG recommendation D1: The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and One Health "lens" when making investments.
 - IACG recommendation E1: The IACG recommends the urgent establishment of a 'One Health' Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat.
 - IACG recommendation E2: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.
- 5. In the following section, we make the case for focusing on these three recommendations and **urge the UN Secretary General to consider these as priorities** for inclusion in his report to Member States (expected in May 2019).
- 6. In the final section, we provide some comments on the other recommendations for consideration by the IACG secretariat as appropriate.

¹ Please note these are listed in alphabetical order rather than in order of importance to the UK Government.

The UK's priority recommendations

IACG recommendation D1:

The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and 'One Health' "lens" when making investments.

- 7. AMR is a complex problem that touches many health, trade, economics, food security, development and conflict issues. Interventions in other areas have a direct or indirect impact on AMR (often referred to as 'AMR-specific' and 'AMR-sensitive' respectively).
- 8. The UK therefore endorses the introduction of an 'AMR lens' in all major investments to support the mainstreaming of AMR across a wide range of sectors, thereby maximising the value of such investments beyond the original intention. We note the benefits of policies such as the World Bank Group's Environmental and Social Framework² and the International Finance Corporation's Policy and Performance Standards on Environmental and Social Sustainability³ where 'lenses' such as gender and diversity and climate change are already being applied on lending/financing decisions. We would strongly welcome the addition of standards that seek to mitigate the impact of AMR, particularly from industries such as agribusiness and pharmaceuticals manufacturing as well as farming, water and sanitation, and healthcare systems infrastructure projects.
- 9. The UK notes that Member States will have a large part to play in working closely with financing institutions to implement any new antimicrobials sustainability standards or to apply an 'AMR lens' when making investments. There is also a place for UN agencies and other bilateral and multilateral organisations to have a significant impact here, without any significant additional cost to them. At country level, UN Country Teams (UNCTs), in partnership with national authorities through UN Development Assistance Frameworks (UNDAF) and Country Programme Documents (CPDs) could have a significant and meaningful role in incorporating an AMR 'lens' across relevant national development priorities. This would also ensure alignment and integration with the new 'Global Action Plan for Healthy Lives and Well-being for All⁴' which recognises that there is currently a gap in the response to AMR within the health-related SDGs.
- 10. It is essential that AMR is addressed as a "whole of UN approach" the UN's ecosystem covers a vast range of functions, areas, goals, populations and diseases, many of which are affected by AMR and its risks. By mainstreaming AMR into the institutions' funding decisions and strengthening the link between the delivery of the 2030 Agenda for Sustainable Development and AMR, investments would become even more sustainable and effective. Furthermore, this would also strengthen the ability of any new 'Leadership Group' (recommendation E1) to integrate AMR as an important consideration within the UN system's own financing activities.

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² 2016. "World Bank Environmental and Social Framework." World Bank, Washington, DC. Available at http://pubdocs.worldbank.org/en/837721522762050108/Environmental-and-Social-Framework.pdf (accessed 15/02/19)

³ 2012 IFC Policy and Performance Standards available at www.ifc.org/performancestandards (accessed 15/02/19)

⁴ See: www.who.int/sdg/global-action-plan (accessed 15/02/19)

IACG recommendation E1:

The IACG recommends the urgent establishment of a 'One Health' Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat.

- 11. Since the historic UN resolution on AMR in 2016⁵, Member States, UN and international organisations and (to an extent) the private sector and civil society have taken positive steps in combatting AMR. Notably, many countries have developed National Action Plans and are now implementing these. However, there is the risk that high-level engagement particularly Member State political engagement will wane if we do not set ourselves ambitious goals for the next chapter in the global response to AMR.
- 12. If we are to progress action faster and further, the wider UN and multilateral system (including the Tripartite Plus⁶) needs to support Member States by giving greater focus and allocating more sustainable, cost-effective and joined-up funding streams to address AMR. Furthermore, these organisations should seek to use the issue of AMR to demonstrate collaborative advantage and economies of scale where working across institutional boundaries can bring significant value-for-money for their respective membership/donors and the citizens they serve.
- 13. We have observed the positive impact that the IACG has had in advocating for a stronger, more joined-up approach to tackling AMR within the Tripartite Plus. The UK applauds the Tripartite Plus's drive to increase coordination and collaboration across the agencies, and we look forward to the finalisation of the Tripartite AMR Workplan this year. However, the UK believes it is essential that the Tripartite Plus's focus on AMR is sustained, and most importantly, scaled up to include other appropriate agencies from across the system to enable a truly integrated 'One Health' approach.
- 14. The UK agrees with the IACG on the need to strengthen coordination across the UN and multilateral system, ensure progress on delivering AMR objectives, and hold the system and Member States accountable for the AMR commitments they have made.
- 15. However, it is important to identify the purpose and value-added of any new 'One Health' Global Leadership Group on AMR before we look at possible structures to deliver this.
- 16. In the UK's view the primary role of any 'leadership group' should be to <u>advocate for collaborative</u>, <u>joined-up actions to address AMR</u>, ensuring it remains a priority for all relevant agencies (in particular the Tripartite Plus), and <u>proposing ways to make these actions more efficient and effective</u> by working across agency boundaries and beyond.
- 17. It should <u>promote and support a cross-agency working culture, at global, regional and country level, and build on other successful UN Global Joint Programmes</u> and multi-

⁵ A/RES/71/3, available at https://digitallibrary.un.org/record/845917?ln=en (accessed 19/02/2019)

⁶ We use "Tripartite Plus" as an informal term for joint working on AMR between the World Health Organisation (WHO), the Food and Agriculture Organisation of the UN (FAO), the World Organisation for Animal Health (OIE) ("The Tripartite") plus UN Environment (UNEP)

agency collaborations. It should <u>help identify gaps</u> in activity and <u>propose areas for improved coordination</u> across the system to fill those gaps. It should have a mandate to promote not just cross-agency but also whole-of-government and whole-of-society action to <u>respond to the AMR-related Sustainable Development Goals</u> as set out in the research commissioned⁷ by the IACG during their tenure. It should help ensure AMR is being well-addressed at country level through ambitious AMR National Action Plans as well as being <u>integrated into UN Development Assistance Framework</u> (UNDAF) documents and agency-specific <u>Country Programme Documents</u> (CPDs) where appropriate.

- 18. Such a function would also <u>help deliver UN development system reform objectives</u> at both global and country levels, the aims of which the UK strongly supports.
- 19. On this basis, the UK does not agree that the proposed structure of the One Health Global Leadership Group on AMR as per the IACG's current draft recommendations would be the most efficient or have the strongest impact.
- 20. The UK could <u>not agree to</u> any new 'leadership group' that takes the form of <u>a new quasi-UN agency with an expensive and complex secretariat and significant infrastructure</u> (i.e. the creation of a 'UN-AMR'). We would consider this to be both unrealistic and unnecessary.
- 21. The UK could <u>not agree</u> to any new 'leadership group' <u>that supersedes or overrides the existing governance mechanisms and structures</u> of each UN or international organisation. Member States must continue to work with each of the relevant agencies to set their individual organisational priorities, agree their budgets and approve their workplans. Any 'group' should therefore <u>not have a mandate to instruct or veto the work of individual agencies</u>.
- 22. Furthermore, the UK does <u>not believe</u> that the response to this recommendation should be fulfilled by either <u>extending the current IACG mandate or duplicating its current structure</u> to form an IACG 2.0. Instead, we should take the best from the IACG's form and design any new 'group' to reflect the most recent thinking on the functions that can best assist the multilateral organisations in delivering across boundaries.
- 23. Instead, the UK proposes that any new One Health Global Leadership Group on AMR should comprise the directors general of the Tripartite Plus agencies and external, independent representatives, supported by a nimble and efficient secretariat which could be drawn from Tripartite Plus agencies. This group should seek input and advice from Member States, UN agencies, international organisations, civil society, and the private sector, as appropriate.

⁷ AMR Indicators and their relevance to the global indicator framework for the SDGs and targets for the 2030 Agenda for Sustainable Development available at: www.who.int/antimicrobial-resistance/interagency-coordination-group/AMR SDG indicators analysis slides.pdf?ua=1 (accessed 19/02/2019)

- 24. We would expect any such 'group' to comprise external individuals who have the credibility and are given the mandate to influence and help drive progress across the UN system, in collaboration with the directors general of the Tripartite Plus. The UK believes that the 'group' should draw upon the views of a diverse range of stakeholders, including the private sector and civil society.
- 25. The work of any new 'leadership group' should <u>be open and transparent</u>. Progress should be <u>reported through existing governance mechanisms</u> of each of the Tripartite Plus members and other relevant institutions, and to Member States, including at country level and through the UN General Assembly as appropriate. The <u>accountability mechanism</u> of the 'group', however, <u>deserves greater investigation</u> from the UN Secretary General and UN Member States before the UK's position can be confirmed.
- 26. If agreed, we would expect the 'group' to be <u>convened as quickly as possible</u> i.e. by the beginning of 2020 so as not to lose momentum.
- 27. The UK also has the expectation that a group would be <u>time-limited but with renewable mandate</u> and whose <u>design and scope is influenced by the best aspects of other structures</u> such as the Global Preparedness Monitoring Board, the Independent Oversight and Advisory Committee for the WHO Health Emergencies Programme, the High-level Advisory Group for *Every Woman Every Child*, the FIA High-Level Panel for Road Safety, the former UN SG's High-Level Panel on Women's Economic Empowerment and the former UN High-Level Panel on Water, amongst others
- 28. If the recommendation E2 is taken forward, there should be a <u>clear link between the</u> 'group' and any independent panel on evidence for action.
- 29. Funding requirements and sources require further consideration, but costs of setting up and running any such group should be minimal. The actual funding mechanism that will be necessary for such a 'group' will require negotiation with Member States and the relevant UN agencies. The UK therefore does not take a position at this stage on what it would and would not consider acceptable in terms of funding source(s), exact budget and length of mandate.
- 30. In conclusion, the <u>UK supports the implementation of a 'global leadership group' if it</u> were shaped to take account of the caveats provided above.

IACG recommendation E2:

The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies [...], UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against AMR in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to AMR, its impacts and future risks, and recommend options for adaptation and mitigation.

- 31. At present, there are still multiple gaps in the scientific evidence base on AMR. In particular, the international community's understanding is limited regarding to the extent to which antimicrobial use in plants and foodstuffs as well as resistant genes present in the environment affect drug resistance in humans and animals. In addition, global surveillance systems and our capacity to track the development of AMR needs to be strengthened. These gaps in our knowledge are impeding the international community's ability to make sound, evidence-based policy decisions. As such, the UK supports the need to improve the evidence base and agrees with the need to establish some type of independent panel which is commissioned by and generates and synthesises evidence for Member States.
- 32. Although plenty of high-quality research has been or is being undertaken worldwide, and clear evidence has already been produced on various aspects of AMR, there is no single mechanism to coordinate a global approach to the development of an evidence base to assist policy-making. Consequently, there is the potential for siloed working, gaps in evidence, duplication, and a lack of global consensus on unified approaches that respond to the evidence base.
- 33. The UK therefore agrees that a new independent panel could ensure the development of a globally-supported evidence base that covers all the many aspects of AMR and practical, cost-effective interventions (both -specific and -sensitive) to address them.
- 34. To ensure the legitimacy of its findings and outputs, the 'panel' would need to include and/or draw upon eminent scientists and researchers across the 'One Health' spectrum and beyond. It should include inputs and evidence from social, behavioural, economic and political sciences.
- 35. The UK would also like to clarify that Member States should be active participants in any 'independent panel'. Member States should be able to commission research from the 'panel' and directly receive any reports that it generates in a similar way to the functioning of the Intergovernmental Panel on Climate Change. This would ensure that the 'Panel's work has a tangible and worthwhile impact on Member States' policymakers.
- 36. This proposal will require further detailed thinking, including on aspects such as the 'panel's' accountability mechanisms (e.g. whether it would be accountable to the 'leadership group' if created per recommendation E1, or directly to Member States), how panel members are selected and how it is sustainably funded. The UK looks forward to shaping these considerations with Member States over the coming months.

Additional UK Government Comments

- 37. This section provides further feedback for each of the IACG's recommendations. The UK noted the IACG's request for feedback to be high level, action-orientated, precise and feasible. We have therefore formulated our response to include:
 - Any small additions or wording changes that would enhance a recommendation;
 - Any recommendation or the considerations for the recommendation which could be challenging for the UK to accept;
 - · Any key gaps in the recommendations; and
 - Whether we consider the recommendation to be feasible and/or implementable.

Section A: Accelerate Progress in Countries

A: General UK comments

- 38. The UK continues to believe that working at individual country level in parallel to any actions taken at a global or regional level can have a significant impact on AMR. As such, we support the philosophy underpinning the IACG's recommendations in section A. However, this is not just about continuing to do the same as has been done until now, but rather seek to create a step-change in the way that AMR is addressed at country level, particularly in low-resource settings.
- 39. We would encourage other Member States to consider using more of their official development assistance to fund AMR-specific and AMR-sensitive actions, in collaboration with the Tripartite Plus agencies and other donors so as to avoid duplication and ensure consistency of approach. This is particularly important in efforts to increase in-country laboratory capacity and capability as well as data collection across the 'One Health' spectrum so systems can be sustainable and inter-operable.

A1: The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health

A1: Suggested addition(s) or wording changes

- 40. For the recommendation summary, the UK suggests a more consistent use of terminology throughout the document when referring to animals, i.e. standardising to "human, animal (terrestrial and aquatic) plant and environmental health".
- 41. For the recommendation summary: the UK suggests using "responsible" rather than "prudent" when discussing antimicrobial use.
- 42. The recommendation summary specifies the role of "licensed professionals", which is too limited in scope. Whilst we note that the text includes this important caveat:

"The IACG recognizes that in settings where trained prescribers are in short supply, non-physicians (such as nurses, paramedics and community health workers) and veterinary paraprofessionals may also be trained and authorized to prescribe or administer some antimicrobial agents."

43. To make it more applicable to many low- and middle-income countries (LMICs) where the role of community health workers is critical, we suggest adding to or changing the language preceding this caveat to read:

"The **responsible** use of antimicrobials across the human, animal **(terrestrial and aquatic)**, plant and environmental health sectors requires appropriate attention to and investment in training, accreditation and regulation of professionals, **including all competent and authorised service providers and/or workers** across [...].

A1: Identified gaps

- 44. For the summary recommendation: infection prevention and control (IPC) is fundamental to the global response to AMR. It is mentioned in the body of the recommendation, but not within the recommendation itself. To raise the profile of IPC and ensure that it is recognised as a key tenet of this first recommendation, we suggest adding it into the wording of the recommendation itself.
- 45. For point (d): we suggest including "waste and water management in health care, manufacturing and farming-related activities" for supporting behaviour change since these are all needed to develop the standards referred to in point (e).
- 46. For point (f): this should also refer to the importance of integrating with disease surveillance (avoiding parallel systems and arrangements) as well as across domains.
- 47. For 'considerations for this recommendation' the lack of access to antimicrobials and other products should be emphasised more with an additional sentence. For instance, "Lack of access in many countries, affecting mainly the poor and vulnerable, remains a major challenge, and responsible for over 6 million preventable deaths."

A2: The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs

A2: Suggested addition(s) or wording changes

48. The UK would encourage the addition of a bullet point within the summary recommendation to acknowledge the need to integrate AMR prevention explicitly into human and animal health system strengthening efforts already underway. This would allow Member States to build capacity on quality of care, infection prevention, medicines management and responsible use and access in a sustainable and systematic way.

- 49. However, should a separate bullet point not be acceptable, we would propose an amendment to point (b) to read: "Strengthening key national systems for human and animal health systems strengthening, infection prevention, monitoring [...]"
- 50. For point (d): the results of the most recent WHO self-assessment survey on progress made on AMR at the country level revealed a clear correlation between multi-sectoral collaboration and progress made. Inter-ministerial collaboration at the national level is therefore key to the implementation of national action plans, and thereby achievement of the goals in the Global Action Plan on AMR. The UK therefore suggests: "Effective national coordination, accountability and governance mechanisms which encourage collaboration between government ministries and sectors."

A3: The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents

A3: Suggested addition(s) or wording changes

51. For the summary recommendation: the UK suggests specifying that it relates to animals (terrestrial and aquatic) as a point of principle. We understand use of antimicrobials for growth promotion in people is currently an accepted practice by WHO in some circumstances in cases of malnutrition.

A3: Identified gaps

- 52. A consideration needs to be added that references how the impact of removing antimicrobial growth promoters could be offset in the short and long term. "Immediate end" does not acknowledge the practicalities of implementation.
- 53. The UK would like to know the (high-level) timescales suggested for eliminating agents other than those which are 'Highest Priority Critically Important'.
- 54. The UK suggests including a sub-recommendation around capacity-building on animal husbandry and welfare for LMICs. This is a laudable recommendation, which the UK supports, but we recognise that many countries may not have the capacity and technical expertise to alter their husbandry practices to phase out use of antimicrobials for growth promotion in current circumstances. Many countries have good, cost-efficient practices that they could share with lower-capacity countries. The Tripartite Plus could and should an important role to play here.

A3: Feasibility of implementation

55. It may be difficult for some countries to implement this recommendation due to infrastructure or economic reasons. Providing case studies to illustrate how this could be achieved under challenging circumstances might help encourage tangible progress.

Section B: Innovate to Secure the Future

B1: The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials - particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials - for human, terrestrial and aquatic animal and plant health

B1: Suggested addition(s) or wording changes

- 56. For the summary recommendation, the UK suggests mentioning the development of compounds that block resistance and thereby extending the life of existing antibiotics within the list "...particularly antibiotics, novel compounds, diagnostics, vaccines...".
- 57. For the fourth 'consideration,' this lists several initiatives for human health. In fact, at least some of these (JPIAMR is a good example) are 'One Health' in focus, and not simply human health. The recommendations should be accurate when describing the examples.

B1: Identified gaps

58. This recommendation focuses heavily on 'push' incentives for developing new antimicrobials. Whilst these types of incentive are essential, it is also crucial that Member States incentivise later-stage drug and product development to ensure any promising discoveries move from bench to bed- or pen-side. The combination of market failure specific to antimicrobial drug development and the continued disinvestment of large pharmaceutical companies in this area is proving catastrophic. Venture capital is increasingly disinterested in investing in smaller biotechnology companies as they see insufficient no longer have larger companies to buy their early-stage compounds to market. Therefore, the recommendations need a stronger focus on developing global *pull* incentives for antimicrobials, including high-level examples of how this could be implemented.

B2: The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health

B2: UK Comments

59. The UK supports the need to focus on access to and stewardship of antimicrobial products as well as tools and techniques across the 'One Health' spectrum. We have no detailed comments apart from a request that the IACG helps prioritise actions considering the very broad nature of this recommendation.

B3: The IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context

B3: Identified gaps

60. The UK suggests adding in a description of how a joined-up 'One Health' approach will be achieved for R&D when a wide range of different stakeholders (public, private, philanthropic) are involved, particularly as their priorities may differ.

Section C. Collaborate for More Effective Action

C1: The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels

C1: Suggested addition(s) or wording changes

61. For point (c): the UK suggests changing the text to "*Provision of support for civil society organisations...*". Explicit calls for Member States and others to provide funding to civil society organisations risks a perception of attempts to co-opt these actors. Their effectiveness as advocacy actors depends on a large measure of independence.

C1. Identified gaps

62. Other groups (for instance learned societies, professional groups) will also contribute to a "One Health" approach and response. These should also be mentioned.

C2: The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels

C2. Identified gaps

63. The value of transparency and sharing learning, for instance through initiatives such as the Access to Medicine Foundation's *Access to Medicines index*⁸ and *AMR Benchmark*⁹ should be highlighted in this recommendation.

⁸ See https://accesstomedicinefoundation.org/access-to-medicine-index

⁹ See https://accesstomedicinefoundation.org/amr-benchmark

Section D. Invest for a Sustainable Response

D1: The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance and One Health "lens" when making investments

D1: Suggested addition(s) or wording changes

64. The recommendation summary needs to be clearer about what the application of a 'One Health' "lens" means – this may not be obvious to many other Member States. In addition, please see the first section in this document for the full detail behind the UK's positions on this recommendation.

D2: The IACG emphasizes the need for increased investment in the global response to AMR. It urges existing and future financing mechanisms in human, animal and plant health, as well as food production and the environment - including Gavi – the Vaccine Alliance, the World Bank, the Global Fund [...], Global Financing Facility, Multilateral Climate Funds, Unitaid, as well as future financing streams for Universal Health Coverage and other priority development issues, and their donors - to give AMR greater priority in their resource allocations. It further calls upon public, private and philanthropic donors in human, animal and plant health, as well as food production and the environment, to increase funding to contribute to addressing AMR, including to support implementation of AMR National Action Plans.

D2: Suggested addition(s) or wording changes

65. Per comment in recommendation A1, language should be consistent when referring to animal health (terrestrial and aquatic).

Section E. Strengthen Accountability and Global Governance

E1: The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat

E1: UK caveats to accepting this recommendation

66. Please see the first section in this document for the full detail behind the UK's positions on this recommendation.

E2: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against AMR in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to AMR, its impacts and future risks, and recommend options for adaptation and mitigation.

E2. Identified gaps

- 67. Please see the first section in this document for detail on the UK's positions on this recommendation.
- 68. In addition, the UK would appreciate further detail and clarification on:
 - a. whether the Panel would conduct its own research or base its analyses on existing research undertaken elsewhere;
 - b. whether the Panel would collect AMR surveillance information across all domains, or whether this remains the role of individual agencies to manage and co-ordinate. It would be useful to have UN-wide agreement on how and who should be collating information across 'One Health' domains;
 - c. to whom the Panel would formally report (i.e. whether this would be to Member States as well as to any Leadership Group);
 - d. who would form the Panel (using more specific examples than what is currently included); and
 - e. the general timescales for implementation.

E3: The IACG requests the Tripartite agencies (FAO, OIE and WHO) together with UNEP and other UN agencies, in the context of UN reform, to further strengthen joint One Health action, based on country priorities and needs, by enhancing their organizational capacity and providing adequate and sustainable core funding for AMR-related activities

E3: UK caveats to accepting this recommendation

- 69. The UK is very supportive of this recommendation, especially sub-recommendation (a) and therefore expects this to be implemented by the Tripartite Plus.
- 70. However, the UK would like to clarify that this recommendation should not be wholly dependent on increased core funding to the Tripartite Plus or other UN agencies. As the UK recently noted during the WHO Executive Board meeting, we expect efficiencies and re-prioritisation to be made internally prior to the Tripartite Plus requesting any additional funding for its work on AMR.

71. In addition, as mentioned in other sections of the UK's comments, we would expect greater coherence on AMR within the Tripartite Plus and other relevant agencies. This includes integrating AMR within the UN's Country Teams' (UNCTs) and UN agencies' work, including at country level through UN Development Assistance Frameworks (UNDAF) and Country Programme Documents (CPDs), as well as within other activities relating to the achievement of the SDGs, including but not limited to SDG 3 and its accompanying 'Global Action Plan for Healthy Lives and Well-being for All'.

E4: The IACG recognizes the ongoing process led by Member States to develop the Global Development and Stewardship Framework to Combat AMR and urges the Tripartite agencies [...] and UNEP to expedite its development in line with the scope described in the 2015 World Health Assembly resolution on AMR (WHA68.7). As Member States finalize this process, they should also consider the need for new international instruments

E4: Suggested addition(s) or wording changes

72. The UK would appreciate clarity (perhaps with examples) as to what "international instruments" the IACG considers could be required, and their order of priority.

E4: UK caveats to accepting this recommendation

73. The UK is open to discussing the possibility of creating future international instruments for AMR. However, we would strongly advocate for the finalisation of the Global Development and Stewardship Framework – focusing very clearly on guidance regarding evidence-based policies on access to and stewardship of antimicrobials, before taking a firm view on whether we could support this part of the recommendation.

United States

Consolidated U.S. Government Response

Draft Recommendations of the Ad Hoc Interagency Coordination Group on Antimicrobial Resistance

General

The United States believes strong and sustained global leadership and advocacy are critical if we are to successfully combat AMR. We thank the IACG for the recommendations and look forward to discussing them with our global partners, as we look forward to pragmatic and effective action that will result in preventing, controlling, and treating AMR.

The United States is supportive of the objective of recommendation E3. WHO Member States recently agreed to a draft resolution to be submitted to the World Health Assembly in May, welcoming the Tripartite agreement on AMR and encouraging greater transparency and engagement with Member States. This resolution asks the Tripartite to work with each other, and UNEP, to establish clear coordination and progress under the joint work plan. The United States believes the work already underway to support and strengthen the Tripartite, UNEP, other international organizations and UN partners, would fulfil the recommendation provided in E3. The United States would also like to express our support of the Tripartite working with other international organizations, such as the World Bank and other UN agencies. We believe combating AMR requires a truly multisectoral approach and this can only be achieved when we bring together all sectors with equities in combating AMR.

The United States is not supportive of creating multiple platforms to provide leadership on AMR. We believe this would provide at best duplicative advice and at worst conflicting advice on how best to address AMR. In addition, the financial cost of supporting multiple platforms and/or secretariats would divert scarce resources from implementation at country level. In this spirit, the United States is not supportive of establishing a One Health Global Leadership Group on AMR. We believe the work outlined in recommendation E1 a – d, and g, could be appropriately led by the Tripartite and its partners. Recommendations E1 f and h fall under requests to the WHO Director General recently called for in the WHO resolution mentioned above. Further, we are not supportive of creating a senior leadership group that would "provide advice and guidance on reports of the Independent Panel" called for in recommendation E2. Concerning E2, particulars of how any platform created by the UN Secretary-General should report its findings, who it should report to, when it should be established, and costing, feasibility and other issues should be discussed by UN member states in New York within the standard procedures of UN processes.

The IACG clearly have expertise regarding the problem of AMR and the necessity of using a One Health approach, as the drafted document makes recommendations touching nearly every aspect of antimicrobial resistance (and use) related to human and animal health, food production (animal and crop), and the environment. Keeping this in mind, the United States suggests additional emphasis on the following priority areas that are underrepresented in the document:

- Risk prioritization so countries can target resources at those areas offering the greatest health impact and outcomes would be particularly helpful.
- The need for research to develop improved methods for infection prevention
- Actions to enhance appropriate use and antimicrobial stewardship, especially given that inappropriate overuse of antibiotics is prevalent both in settings where antibiotics are available by prescription and over the counter
- Optimizing the use of existing antimicrobials

Recognizing the opportunity that the current technological revolution affords, we encourage the IACG to look at innovative and novel approaches to the effective prevention and control of avoidable antimicrobial resistance and the importance of enhanced focus on applying these advances toward that end.

The United States notes that, while various individual agencies, organizations, and foundations are explicitly called out in the recommendations, they are not exhaustive of the many valuable organizations that are and will be important and involved in the fight to combat AMR.

Finally, it would be useful to include a definition of the scope of the AMR threat, as well as what classes of compounds are included under antimicrobials, to make clear that antimicrobials are being considered in the broader context to combat fungal, bacterial, parasitic, viral, vector-borne, and zoonotic diseases.

Specific

First paragraph:

• Sentence stating, "...explore the feasibility of developing global goals and targets related to antimicrobial resistance...": The science and circumstances on this issue vary greatly between countries (prevalent diseases/pathogens, affected species, susceptibility patterns, varying source attribution, accessibility, regulation, changes in population size and disease conditions) and do not lend themselves to global targets. Developing global targets seems inappropriate in this case and outside the mandate of the IACG.

Page 2:

Paragraph 1:

• References and citations for the numbers listed would be very helpful to better understand where the calculations are coming from. From our understanding, the

O'Neill report listed 10 million per year by 2050, and we are under the impression that the models in the O'Neill report estimated closer to \$1.1 trillion on the high end for total annual shortfall – based off of total GWP estimated at \$75 trillion and the O'Neill "1.4% smaller by 2030"

• "The total annual shortfall in gross domestic product (GDP) due to antimicrobial resistance could be as high as \$3.4 trillion by 2030, equivalent to the losses experienced during the 2008 global financial crisis." This is a challenging comparison as the markets have come back. The proposed GDP shortfall would be much harder to replace, as lives lost and a disabled workforce due to AMR would not be as resilient and unable to work to rebuild the GDP loses.

Paragraph 2:

- We would like to note that the overuse and misuse of antimicrobials is not limited to agriculture but significant in human medicine as well. Effective stewardship of antimicrobial use needs to be optimized in all sectors.
- First sentence:
 - o It may be worthwhile to further include environmental contamination with antimicrobials from pharmaceutical production, as well as effluvia from human and animal wastes.
 - o It may be helpful to clarify what good agricultural practices means.
- Last sentence:
 - Causality is an assumption and implies that we can quickly "fix" things. Recommend alternative language: "As a result of decades of poor stewardship of antimicrobials and these contributing factors, documented cases of drug-resistant infections have increased across the globe and treatment options are worryingly limited and ineffective."

Page 3:

• Bullet 3: Suggested edit: "...country and disease-specific contexts..."

Justification: Addressing MDR TB is different from addressing fungal disease or AMR bacteria.

Recommendation A1:

- The access needs of each member state will be different. Prudent use and good antimicrobial stewardship practices, along with a call for better diagnostics, could improve the accuracy of prescribed antibiotics in all countries.
- Letter e: Suggested alternative language: "based on international best practices and standards for: equitable access..." as we are not aware of international standards for equitable access
- Recommend adding an additional action item to develop best practices for and increased adoption of antimicrobial disposal and waste management.

Page 4:

- Sub-Bullet 1: Consider noting the importance of following intellectual property protections.
- Sub-Bullet 2: Consider the feasibility of this recommendation for bacterial infections as establishing these forecasts, even within countries with robust public health and pharmaceutical reporting and surveillance, would likely be extremely burdensome at the level of detail needed to provide actionable information.
- Sub-Bullet 3: "Establishing antimicrobial production facilities" is both financially and logistically extremely challenging. More appropriate and effective recommendations to enhance access are listed within the recommendations.
- Sub-Bullet 6: Regarding "efforts to ensure Universal Health Coverage", consider elaborating where and how these efforts will be focused.

Page 6:

Bullet 1:

Regarding the statement, "...easily compared, exchanged, used and aggregated locally, nationally and globally." The complexities of data generation, storage, reporting, and exchange should be taken into consideration. Consider further elaboration on specific platforms to use for comparing, exchanging, and utilizing data as well as type of reporting (phenotypic, genotypic, etc...). Finally, consider including 'verifiable' when discussing data, because while sharing data among countries is important, unverified data could prove counterproductive in this effort.

Recommendation A3:

• Bullet 1: In recognition that antimicrobials are critical tools for animal health that, like antimicrobials for humans, need to be preserved for the long-term, suggest addition of: "The IACG recognizes that the use of antimicrobials in animal production is critical for animal health, food security and economic stability. The appropriate use of antimicrobials in animal health is important for promoting the long-term utility of antimicrobial agents in animal health and in promoting human, animal, plant and environmental health and food security. The use of antimicrobials in animal production may be as high..."

Bullet 2:

Application of antibacterial compounds in crops is dependent on factors such as
the susceptibility of the crop to the pathogen; the prevailing environmental
conditions conducive for disease development; and the aggressiveness/virulence
of the strain of bacteria in a given geographic location. Use of antibacterial
compounds in plant agriculture is not applied as a plant growth promotion
material, but used as a first line of defense to reduce bacterial concentration in the
overall bacterial disease management program.

Bullet 3:

• The United States supports risk analyses and their intended use to better inform decision-making. Please elaborate on how and who will help support these efforts as resource challenges may prove very difficult to overcome, and how these risk analyses should be used to implement goals.

Page 7:

Recommendation B1:

- Bullet 2: Consider adding more clarity and detail on the principles listed.
- *Bullet 3:* Suggest defining and elaborating on what non-financial market incentives are, as they are mentioned a number of times in the document.
- Suggested addition of: "c. Leveraging and applying technological advances across the spectrum of need, including novel and innovative approaches that enhance action throughout the world recognizing the diverse local contexts globally."

Page 8:

Recommendation B2:

- Bullet 1: Please clarify how existing initiatives in other areas such as AIDS and malaria can be leveraged for antibiotic development.
- *Bullet 2:* Please elaborate on where funding for the "new global initiatives" will come from.

Page 9:

Recommendation B3:

- Consider noting the importance of following intellectual property protections within efforts to enhance collaboration and information sharing. Rights around proprietary information and data sharing should be protected and respected.
- *Bullet 2:* We are supportive of efforts that aid informed decision making on how to invest resources, but want to ensure that external entities do not make decisions for others.

Page 10:

Aim of the recommendations in this section:

Suggest more explicit language on the involvement of UN agencies and entities.

Recommendation C1:

- Bullet 2: Since AMR is a multisectoral issue, examples and reference to AMR related issues should be reflected as such. Consider adding human and animal health to this section.
- Bullet 4: We recognize the importance of involving civil society in advisory councils, community advisory boards, etc., and understand that support to enhance their engagement can take many forms (not only financial).

Page 11:

• Recommendation C2 is critical and we recommend it be placed higher.

Page 12:

Recommendation D1:

• Bullet 2: While an analysis of how the response to AMR contributes to achieving the SDGs is important, resources allocated to combatting AMR may not have the capacity to take on this effort. Suggest locating resources in existing projects aimed at achieving the SDGs to contribute to this effort.

Page 13:

Recommendation D2:

• Bullet 4: We are supportive of efforts that aid informed decision making on how to invest resources, however want to endure that external entities do not making decisions for others outside of suggestions.

Page 14:

Recommendation E1:

- As stated above, the United States does not support the permanent establishment of this group as recommended in the current draft. We believe these functions can be fully captured within an empowered, transparent and inclusive Tripartite plus. We also question the need for an external secretariat. How would this new secretariat, if the One Health Global Leadership Group was formed, interact with the Tripartite?
- The recommendation states the need for global governance and establishing a One Health Global Leadership Group, with funding from multiple sources, to address the issues from a global perspective. A major concern with this is the addition of another layer of governance where there are already multiple initiatives and efforts underway. The efforts of the Tripartite could appropriately lead these suggestions.

Addendum to Consolidated U.S. Government Response

Draft Recommendations of the Ad Hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance (AMR)

In the response to the IACG call for public comments on the draft recommendation, the United States highlighted our support for the objective of recommendation E3. We believe it is critical to maintain leadership on AMR in the International Organizations (WHO, OIE, FAO) as each have a clear mandate, expertise, and an established governance structure appropriate to combating AMR with a One Health approach. We encourage IO leadership to support combating AMR at the highest political levels and to engage or continue to engage other international organizations, such as the World Bank and other UN agencies including UNEP, on these efforts. To reiterate, the United States believes the work already underway to support and strengthen the Tripartite, UNEP, other international organizations and UN partners, would fulfil the recommendation provided in E3.

The United States is not supportive of creating a One Health Global Leadership Group (E1) as currently described in the draft recommendation. The United States is not supportive of creating any leadership group to oversee or dictate policy, agenda or action to the International Organizations and the Tripartite work plan. However, we do think there is a role for eminent persons to provide advice and guidance to the Tripartite. The United States would be supportive of adapting the recommendation for a One Health Global Leadership Group on AMR called for in E1 into an advisory group of eminent persons who could provide feedback, advice, and recommendations to the Tripartite and its partners (E3). In recognition of the multi-sectoral nature of the challenge, this group could work out of NY under the auspices of the Secretary General, but operationally and substantively be guided, supported and managed by the Tripartite.

As stated in our initial feedback, the United States believes combating AMR requires a truly multi-sectoral approach and this can only be achieved when we bring together all sectors with equities in combating AMR. An eminent persons advisory group should consist of experts from all sectors who have equities in AMR, including NGOs, academia, and the private sector. It could include AMR subject matter experts from public health, agriculture, finance, human and veterinary medicine, food safety, drug development and manufacturing, implementation science and behavior change, and other relevant disciplines. A benefit of this group would be its ability to encourage action and provide much needed independent and external insight into combating AMR.

The United States uses a similar mechanism that has proven essential in advancing work to combat AMR under the U.S. National Action Plan for Combating Antibiotic Resistant Bacteria (CARB). The CARB Federal Taskforce, which consists of AMR experts from government agencies and is responsible for U.S. policy decisions on AMR, the U.S. National Action Plan content, and implementation of a One Health approach to combating AMR, is advised by the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB). This eminent persons group, whose expertise spans the breath of multi-sectoral equities on AMR,

strives for regional diversity and contains both voting and non-voting members as dictated by its charter. More information is available at https://www.hhs.gov/ash/advisory-committees/paccarb/about-paccarb/charter/index.html

For recommendation E2 we propose an additional option for consideration. The United States strongly endorses the concept of providing on-going, credible, scientific evidence on AMR research, gaps, and recommendations to address scientific need and to galvanize action. The Tripiartite could fulfill the objective of E2 by tasking the Interacademy Partnership (IAP) with this work. The IAP has a membership of 138 academies of science, medicine and engineering from around the world; these include both national academies/institutions as well as regional/global groupings of scientists and a number of other scientific organizations participate in IAP meetings and activities as either observers or partners. The IAP has over sixty years of experience in providing advice to governments on health and science policy, and it has an existing health track, including One Health committees, and has already worked on the SDGs. We believe there is value in utilizing existing, established bodies with successful records of accomplishment, rather than creating new structures, which requires significant time and expense. In addition, the IAP has reach into academies' experts across the globe, thereby providing critical knowledge of local contexts to ensure practicable and relevant advice. When taking recommendation E2 forward, we also request that a clear consultative process inclusive of Member States and other stakeholders be followed, using established UN practices for such consultations to ensure buy-in and support to any outcome. In our view, because the Tripartite organizations already account for the inter-governmental response to AMR at global level, an approach to E2 does not need to include an explicitly inter-governmental outcome in its structure, though this is also a potential benefit to pursuing the IAP option we have proposed.

ANTIBIOTIC RESISTANCE
COALITION (ARC) RESPONSE
TO THE PUBLIC
CONSULTATION ON THE
DRAFT RECOMMENDATIONS
OF THE INTERAGENCY
COORDINATION GROUP ON
AMR (IACG)

February 2019

Signatories

Alliance to Save Our Antibiotics Center for Science and Environment Consumers Association of Penang **Ecumenical Pharmaceutical Network** European Public Health Alliance Food Animal Concerns Trust Friends of the Earth Malaysia Health Action International **IFARMA** Foundation *Institute for Agriculture and Trade Policy* Oceana People's Health Movement ReAct – Action on Antibiotic Resistance ReAct Africa ReAct Asia Pacific ReAct Europe ReAct Latin America ReAct North America Society for International Development Third World Network Universities Allied for Essential Medicines

Overarching Feedback

- The Antibiotic Resistance Coalition urges the IACG to communicate to policymakers reading its final recommendations that:
 - The need to respond to the challenge of antimicrobial resistance is urgent
 - Resources--both financial and technical--must be commensurate with the call for action on AMR. A stronger case for investment, including for capacity building, should be made.
 - Targets must be set, both globally and at the country level, so that milestones might be measured and met in addressing this challenge in a timely manner.
 - Accountability for meeting these milestones must be put into place.
- We need recommendations that will move the world forward, not just reiterate what has
 already been proposed in previous reports. So the value added of the IACG's recommendations
 should be clearly stated.
- To address the intersectoral dimensions of this challenge, the report should take a **systems perspective** of how the recommendations fit together.
- Conflicts of interest must be addressed at all levels of the recommendations where industry is suggested to play a role or contribute in global governance, financing, and implementing interventions on stewardship or access.

I. National Action Plans

Recommendation A2 should provide next steps to advance National Action Plans (NAPs) on AMR. To be practical and feasible, it should pull more concrete proposals from the IACG discussion paper on National Action Plans, which are currently not fully reflected. Currently the recommendations are very broad, so they seem to cover everything and nothing at the same time. We need a systems perspective or theory of change to have impact.

There is a clear disconnect between the guidelines put forth in the Global Action Plan and National Action Plans and in-country practitioners who are often unaware of the NAP guidance. Similarly, they are often unaware of the SDGs agenda and its links to AMR. Governments have the responsibility to ensure the flow of information so that practitioners across sectors have this information available to them. Therefore, the IACG should make a stronger commitment to support communications and behavior change interventions. As proposed in the discussion paper on *Meeting the Challenge of Antimicrobial Resistance: From Communication to Collective Action*:

- Licensing and credentialing could support behavior change by increasing healthcare provider training on the prudent use of antimicrobials.
- Networks of similar institutions sharing the same challenges could be useful platforms to support
 peer-to-peer learning, share of best practices, and set milestones for tackling AMR among farms
 and hospitals.
- Through stakeholder engagement and empowerment, countries should create networks of crosssectoral national experts and champions to drive NAP implementation
- Platforms should be established for coordinating and amplifying communications.
 Intergovernmental agency forums could coordinate global AMR communications to networks of

- stakeholders. Open knowledge-sharing forums such as a global repositories of campaign materials and effective tools for NAP implementation could help share best practices.
- Intergovernmental organizations through a shared platform at country level could provide NAP implementation support and share information of their activity implementation focus areas to complement and prevent duplication but also reinforce other global agendas.
- A coordinated research agenda should be established to drive effective behavior change, communications, and incentive structures.
- Primary health care settings play an important role in facilitating education and shifts in behavior and attitudes towards antibiotic use among local communities. Primary health care settings should therefore be considered central to implementing stewardship efforts.

Mainstreaming, financing and regional cooperation, the three areas of recommendation put forth in the IACG discussion paper on National Action Plans, should be emphasized in Recommendation A2.

- Mainstreaming AMR into broader universal health coverage, sustainable development, infection prevention, food system and environment agendas is key, both to scaling and to sustaining efforts to address AMR.
 - a. UN agencies such as UNICEF and UNDP and other intergovernmental organizations should be engaged in NAP development and implementation work.
 - b. The AMR lens can be applied to a range of existing development campaigns as AMR resonates across sectors and issues including universal health coverage (UHC), WASH, Infection Prevention and Control (IPC), nutrition, vaccination coverage, infectious disease control and sustainable agriculture.
 - c. The UN and Tripartite agencies have recognized the need to address AMR as part of achieving the Sustainable Development Goals (SDGs). AMR should be clearly integrated into the SDGs through specific targets and indicators aligned with the goals and targets outlined in the global action plan. This would help ensure commitment of financial and technical resources from both Member States and UN agencies as well as allow for further monitoring of NAP implementation. With regards to food systems, tackling AMR should be addressed in SDG2 (Zero Hunger), but also in SDG12 (Responsible consumption and production).
- 2. **Financing**: Member States need to dedicate funding to NAP implementation. Sustainable financing for AMR should include support for the implementation of stepwise approaches, prioritization of resources, and access to essential antibiotics. The need for increased funding for NAPs should be emphasized in Recommendations A2 and D2.
 - a. In developing a plan for NAP implementation, countries should be supported in mapping of various stakeholders, programs and funding streams for AMR at the country, as well as state and province level, as is suggested at the global level in Recommendation B3.
 - b. Support towards implementation, operational and translational research for countries that will support improved practices to address AMR

- c. Insurance-based model of financing should be coupled with efforts to avoid overtreatment and overdiagnosis
- d. The IACG could call upon intergovernmental agencies to help provide a prioritization framework to assist with country-level decision making and assessment of return on investment from different AMR interventions. Even those with minimal domestic resources, can commit to a core set of actions on AMR, such as the establishment of an Inter-Ministerial Committee to coordinate implementation of the NAP on AMR. The interministerial Committees could also include developmental partners to maximize resources.
- 3. **Regional cooperation:** The Tripartite, UNEP and other UN organizations should provide guidance and support to countries to help create national governance bodies and mobilize national and local networks to support NAP implementation. This should be tied to the call for increased global guidance and support in Recommendation E3.
 - a. Global governance structures should provide technical support across sectors and themes, including awareness raising, knowledge building, surveillance, stewardship and infection prevention and control (IPC).
 - b. The recommendations should push for greater Civil Society Organization involvement in the implementation of NAPs, given their important role in ensuring transparency and accountability in the NAP implementation process.
 - c. There should be a ban on industry mismarketing of antimicrobials and the establishment of stronger regulatory systems. In particular, governments must restrict pharmaceutical companies' rights to market and advertise antimicrobial products for use in food production, banning the promotion of antimicrobials directly to farmers and food animal producers, especially in LMICs.
- 4. **Targets:** The IACG should call on countries to set clear targets for NAP implementation and support the strengthening of global and national surveillance systems.
 - a. Setting measurable targets will be important for establishing priorities for action and resources and for supporting monitoring and accountability efforts. There should be targets for access to antibiotics, curbing excessive use, and lowering drug resistance levels.
 - b. Data and increased surveillance is urgently needed. Local surveillance and consumption data will be necessary to establish country progress towards reaching set targets for NAP implementation. In countries lacking a strong surveillance system, point prevalence studies can provide a snapshot of the country situation when it comes to resistance levels, antibiotic use, availability and affordability of antimicrobials.
 - c. Targets should also be set for awareness. In India, despite efforts to involve a range of stakeholders, less than 50% of States participated in NAP launch due to the lack of awareness
 - d. A tiered approach to target setting might convince lower resourced countries to participate in the global reporting system at an earlier stage. Rather than a "one size fits

all" approach, both indicators and programs could lay out a series of country-level targets and stepping stones, taking into account the country's assets and resources and with expectations growing as local infrastructure and capacity do and as external technical and financial support is received.

- 5. **Access**: The IACG should make a stronger commitment to support sustainable access to quality, affordable antimicrobials at the country level through effective use of health information, health care financing, strong supply chain systems, and pharmacovigilance. Recommendation B2 should support access efforts at the country level.
 - a. Ensuring affordable access to antibiotics and other health technologies is crucial, so we strongly support the promotion of government-owned production and pooled procurement as mechanism to ensure stable supply and affordable prices.
 - b. We commend the recommendations' emphasis on access and on associated efforts including WASH, IPC and vaccination.
 - c. The considerations under Recommendation A1 mention the need for surveillance systems to include indicators for monitoring access, availability and affordability. The recommendations should more clearly call for *country-level* indicators to monitor access, availability and affordability.

II. Curbing antimicrobial use in animal production

- The IACG Recommendation A3 should include proposals for ending all routine farm antibiotic
 use, including in particular all purely preventative group treatments, in line with the new EU
 legislation and the WHO recommendations. We support IACG efforts to phase out
 antimicrobial use for growth promotion, but the recommendations on this point should be
 strengthened.
 - a. We agree with the IACG that "the overuse and misuse of antimicrobials to promote growth and routinely prevent disease in healthy animals and crops without appropriate indication and the absence of good agricultural practices are contributing to the development and spread of antimicrobial resistance in both animals and humans" [bold added]. We are therefore surprised and disappointed that the report recommendations fail to address the issue of antibiotics being used for routine disease prevention and are insufficiently strong regarding their use for growth promotion.
 - b. The IACG recommendations do not address the use of antimicrobials in disease prevention. As the use of antimicrobials for both growth promotion and disease prevention in food animal production do not require the diagnosis of disease, not dealing with disease prevention in curbing antimicrobial use opens the door to food producers justifying antimicrobial use for disease prevention, just relabeling such use from growth promotion. The experience of European countries has shown that just banning growth promotion does not result in meaningful reductions in overall antimicrobial use in food production. The recommendation is incomplete without the mention of disease prevention.

- c. The recommendations call for phasing out of antibiotic use for growth promotion consistent with Tripartite guidance, but the various forms of guidance are inconsistent. WHO's guidelines on the use of antimicrobials in food animal production are, however, very clear: "We recommend complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion." In addition, all three Tripartite organizations, WHO, FAO and OIE, stated that antibiotics in animals should be "only used to control or treat infectious diseases and under veterinary supervision" in their WAAW 2015 promotional materials, thereby condemning antibiotic use for growth promotion or disease prevention.
- d. The European Union phased out growth promoters between 1999 and 2006. However, in many Member States growth promotion was substituted by increased use of preventative group treatments, a shift that was relatively straightforward to achieve since in both cases there is no need for any disease to be diagnosed before a group treatment is given. As a result, overall farm antibiotic use remained very high and antibiotic resistance in livestock continued to increase (see e.g. "MARAN 2007"). Superbugs such as MRSA, ESBL E. coli and fluoroquinolone-resistant Campylobacter became much more widespread in European livestock after the growth-promoter ban (see e.g. reports "European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks" for 2005 to 2017). As a result of the failure of the EU growth-promoter ban, the EU has now decided that there is a need to impose far greater restrictions on antibiotic group treatments: from 28 January 2022, in the EU all antibiotic preventative group treatments in livestock will be banned. The WHO guidelines on farm antibiotic use also support an end to routine preventative use.
- 2. Recommendation A3 calls for putting an end to use of Highest Priority Critically Important Antimicrobial Agents (HPCIAs) for growth promotion, but greater restrictions are required on the use of these antibiotics in livestock.
 - a. The HPCIAs the fluoroquinolones and the 3rd and 4th generation cephalosporins should never be used for disease prevention or for any form of group treatment. They should be reserved solely for the treatment of individual sick animals where sensitivity testing shows that other antibiotics would be unlikely to work. The last-resort antibiotic colistin should be completely banned from farming worldwide due to clear evidence that use in livestock is contributing to resistance in human infections.
 - b. Recommendation A3 should extend the phase out of growth promotion to all medically important antibiotics, not just Highest Priority Critically Important Antimicrobial Agents (HPCIAs). Ideally, no antibiotics, whether they are medically important or not, should be used for growth promotion. Even currently non-medically important antibiotics can potentially co-select for resistance to medically important antibiotics. Other adverse effects from routine use of antibiotics include increased salmonella shedding, increased number of potentially pathogenic E. coli in animals' guts, toxic residues, and environmental pollution. However, at a minimum, all medically important antibiotics should be banned for growth promotion purposes.

- c. The <u>new policy from McDonald's on its top ten beef-sourcing countries</u> is an example where the ban has been extended to all medically important antibiotics: "Use of Antibiotics defined by WHO as Medically important antibiotics for human medicine are not permitted for the purpose of growth promotion in food-producing animals in McDonald's Supply Chain."
- 3. To cover points 1 & 2 above, we support the following rewording of Recommendation A3: "The IACG calls on Member States to reduce use of antimicrobials in food animal and plant production with targeted reduction goals determined by countries' specific conditions.
 - Member States should end use of medically-important antimicrobials for growth promotion purposes consistent with WHO's Guidelines on Use of Medically-Important Antimicrobials in Food Producing Animals.
 - In addition, Member states should end use of MIAs for disease prevention purposes, except where a veterinary professional judges there is a high risk of spread of a specific infectious disease, based on a recent culture and sensitivity testing results. Antimicrobials should only be used to treat or control disease, consistent with the guidance of tripartite agencies (FAO, OIE and WHO).
 - Finally, use of Highest Priority Critically Important Antimicrobials (i.e., quinolones, thirdand higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymixins) should immediately end for growth promotion, disease prevention and disease control in food animal or plant production and should be permitted for disease treatment only if it is the only treatment option as determined by recent culture and sensitivity testing results."
- 4. The reliance on risk analyses to justify the removal of antimicrobial use for growth promotion is unnecessary, unjustified, and unsupportable in resource-limited countries. While OIE has taken a position against the use of antibiotics in growth promotion in the absence of risk assessment, resources to conduct such risk assessments may not be available in many countries, and importantly, it is unclear why this exception exists as antibiotic use for growth promotion should always be banned, as supported by the evidence laid out in the WHO guidelines. And, if such risk analyses are conducted by parties with a vested interest in the outcomes, the results could be biased.
- 5. Recommendation A3 fails to call for data transparency and target setting and to highlight the need for overall reductions in antibiotic use in food production.
 - a. Recommendation A3 should emphasize the need for data transparency by stating that it should be mandatory for all companies and Member States to make publicly available their data on antibiotic use in food production.
 - b. Targets for reducing of antimicrobials in food production need to be country-specific, as setting such targets and striving towards milestones can be a key ingredient for success. For example, targets have greatly contributed to large reductions in farm antibiotic use in

- countries such as the Netherlands and Norway, and are currently contributing to reductions in the UK and Belgium.
- c. It is important to note that, as access to formalized veterinary care is limited in many low-resource settings, the same set of standards cannot be applied to across countries.
 Therefore, timelines and country-specific targets for phasing out antibiotic use could differ among countries.
- 6. The IACG document should recognise that intensive farming systems contribute to poor animal health and welfare, and to high levels of farm antibiotic use. We welcome the IACG statement (p. 3) that good animal welfare contributes to infection prevention and control on livestock farms. However, the IACG recommendations should include greater emphasis on how to improve animal health and welfare.
 - a. Vaccination, clear water and hygiene are all appropriately mentioned, but the need to move away from industrialised farming systems is not considered. The UK government's Review on Antimicrobial Resistance and the European Food Safety Authority and European Medicines Agency have all highlighted that antibiotic use tends to be much higher in intensive systems. In contrast, antibiotic use in pasture-based systems can be a small fraction of use in more intensive systems.
 - b. Financing mechanisms should be established to aid smallholder producers in making the transition to more sustainable practices, both in the animal and plant sector. Several mechanisms are proposed in the considerations of recommendation D1, but we would add a specific transition fund for small-sclae producers and economic incentives, and lift up these points to the Recommendation level. The considerations under A3 should also point to the need for such financing mechanisms to enable the implementation of the recommendation.
- 7. In Recommendation B2 on future global access, the considerations should distinctly say that alternatives include new compounds as well as practices, such as improved animal husbandry, sanitation, integrated pest management, soil health and crop rotation.
- 8. In Recommendation C1, consumer organizations should be included alongside civil society. With increased financial support, consumer organizations can continue to advocate for responsible antibiotic use in agriculture. In the considerations, we suggest adding: "Providing funding could enable sharing of strategies among consumer and other civil society organizations to bring pressure in the marketplace to increase availability and sales of food from production systems than minimize or eliminate use of antimicrobials, especially medically-important antimicrobials."
- 9. We strongly support the creation of the Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context, as called for in Recommendation E2. This would provide much needed guidance across intergovernmental agencies on how best to weigh available evidence and to adopt policies to address AMR. This panel should draw on the

experiences and lessons of similar existing entities. In particular, the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD), a global scientific assessment initiated by the World Bank and the United Nations, is a valuable example.

III. Innovation & Access

- 1. The strategic targeting of R&D incentives in Recommendation B1 should be based on an analysis of gaps, opportunities, and potential returns on investment and should target innovation both of technologies and of practice.
 - a. The focus should not exclusively be on bringing new antimicrobial drugs to market, but also on repurposing older antibiotics, adapting existing drugs to specific local needs, exploring the role of combination products, R&D of new diagnostic and vaccine technologies, and piloting and scaling of improved antimicrobial use practices. Effective alternatives are mentioned in Recommendation B1, but this wider range of much needed approaches to innovation should be acknowledged.
 - b. Going beyond product development, innovation should encompass implementation, operational and social science research. While recognized in the last consideration, the need for such efforts should be lifted up to the main text of Recommendation B1.
 - c. It is unclear what "accelerate clinical trials in humans, animals and plants" means. Better phrasing may be "finding out which clinical trials are essential for advancing human health."
- 2. The considerations of Recommendation B1 should propose **concrete mechanisms for funding this range of research,** as the existing international mechanisms for research and development do not cover all the necessary focuses.
 - a. Transparency should be a condition tied to the funding for AMR research to accelerate innovation. All clinical trials results should be publicly accessible and publications should be published open access.
 - b. The current initiatives listed in the considerations for B1, for which the IACG "recommends full and sustained funding," may not be the only or best initiatives to fund. Money for AMR may not be best spent replenishing CEPI and IMI (and CARB-X), and initiatives such as GARDP and GAVI should be considered as well in an effort to support sustainable innovation and access and vaccine development, respectively. In particular, CEPI does not have a policy specifically on affordable access.
 - c. An independent analysis should be conducted before resources and funding are committed to any specific initiative. Funding to new or existing initiatives should follow the UN Political Declaration principles and be needs-driven, evidence-based and guided by the principles of affordability, effectiveness, efficiency and equity.
- 3. Recommendation B1 should emphasize that incentives for innovation should focus on the scientific bottleneck of early drug discovery as well as address market and structural barriers to ensuring affordable and equitable access to health technologies needed to address AMR.

- a. The mention of the need to 'pull new products through to market and ensure effective stewardship' overemphasizes the role of pull incentives. Focusing only on pull incentives will not address adequately the serious scientific bottleneck in the discovery of novel classes of antibiotics nor improved access to old, existing drugs.
- b. The considerations under recommendation B1 note that the lack of new antibiotics, diagnostics and vaccines is due to "unclear market potential [...] primarily due to the **high cost of research and development**" but this is not accurate.
- c. What is meant with "non-financial incentives"? Further IP incentives or transferable exclusivity vouchers should not be considered as they would put access to new drugs at risk.
- 4. We endorse the IACG's alignment with the guiding principles laid out in the 2016 UN Political Declaration on AMR. However, Recommendation B2 on equitable and affordable access remains weak and unspecific, and it should more strongly push for a global access initiative.
 - a. In addressing R&D and access, the recommendations successfully highlight the need for "equitable and affordable access and stewardship" and affirm that "all research and development efforts to address antimicrobial resistance should be needs-driven, evidence-based and guided by the principles of affordability, effectiveness, efficiency and equity."
 - b. However, the principle of delinkage is completely missing from the recommendations, despite being put forth in the UN Political Declaration. The recommendation could specify that all the principles already agreed upon by the Member States in the UNGA Political Declaration should be followed.
- 5. It is of particular importance to have a full picture of the AMR R&D landscape to inform global decisions on investments needs. Monitoring of global R&D efforts should lead to identifying the areas of greatest need, which in turn should inform investment decision making by funders. The call in Recommendation B3 for "undertaking coordinated global mapping of research and development activities" would benefit from being developed further in the considerations.
 - a. For the new mapping initiatives to have credibility and be of use for priority setting and decision-making, it should be comprehensive, accurate and cover the full R&D and investment landscape. This requires going beyond the narrow focus on drug development and also capture data on the R&D landscape and funding streams with a One Health approach for the development of relevant diagnostics, prevention measures and technologies including vaccines and overlooked areas such as innovation in healthcare delivery systems, capacity building, social sciences, and improved clinical practices in human and animal health.
 - b. The efforts to map research initiatives should employ a global lens, and there is a need to seek broader inclusion and buy-in from more LMICs in these initiatives. The current examples listed do not meet these requirements for a truly global mapping, as their interest sphere is targeted at high-income countries and on human health and health

technology interventions and, therefore, do not necessarily give a holistic view of innovation.

6. Stating that we should "build upon existing R&D efforts" in Recommendation B3 does not transmit the urgency to invest in R&D and gives the impression there is an existing good pipeline that simply needs more backing. Access and stewardship requirements should be emphasized in the push for increased R&D investment.

IV. Civil Society and Private Sector involvement

- We commend the IACG for supporting civil society organizations (CSOs) and emphasizing their important role in monitoring and accountability in Recommendation C1. CSOs should receive increased political, financial and technical support for their efforts. CSOs also have an important role in ensuring transparency and accountability in the National Action Plan implementation process, so the recommendations should push for greater CSO involvement in the implementation of NAPs.
- Civil society groups should be more clearly defined as they cover a broad range from
 professional societies to trade unions. The specific mention of farmers' groups, consumer
 organisations and stakeholders from environment sector which are traditionally underrepresented in debates around AMR action is positive.
- 3. The recommendations should advocate for strong horizontal and vertical integration between various allied sectors involved in strategically important action at various levels of governance and strive for synergistic action among civil society groups who may have better resources, community access and visibility. In many countries (such as India) CSOs's watchdog role over transparency and accountability has been challenged and governments have created hurdles to civil society, which these strategies would help overcome.
- 4. It would be important to highlight in Recommendation C2 the problems with private sector engagement in solving issues related to misuse of antibiotics, access and equity and to instead highlight the role of the public sector in addressing access and equity. Pharmaceutical companies have significant financial conflict of interest, and promoting the prudent use of antimicrobials could amount to marketing. We support the inclusion of a clear recommendation to address the incentive structures that distort the market and promote inappropriate antibiotic sales and use.
- 5. **Explicit safeguards against financial conflict of interest should be included in the recommendations**. These safeguards should include structural mechanisms to differentiate between social responsibility and commercial interests. The recommendations shouldn't be used to legitimize commercial interests packaged as philanthropic initiatives. Recommendations like

this from a high level body can be misused on the ground by commercial entities for profit making, unless definite safeguards are put in place.

- 6. Benchmarking and transparency in the implementation of industry codes is essential to enable self- and external monitoring.
- V. Sustainable financing and accountability
 - The structure of the recommendations could more clearly show that investments fall into three
 major categories: acknowledging and better channeling the existing funding that goes to AMR;
 applying an AMR lens to existing funding streams and approaches; and highlighting the need
 for new financing mechanisms.
 - a. The recommendations should call for the existing resources to be better channeled. Currently countries are already spending money on treating severe infections and therefore we should recognized these existing costs as part of AMR investments. There should be a better allocation of the money and investment into more cost effective strategies such as IPC and improving health care systems. There is also a need to make the economic case to show the current cost of not taking action.
 - b. The "AMR lens" is a powerful tool that is important to create awareness and that should be applied to existing funding initiatives. However, we need to ensure that we do so with a clear strategy to measure results and that the effort is directed at areas where it will make a real difference and have an impact in tackling AMR issues.
 - c. The push for new financing needs to be stronger in Recommendation D2. The recommendations should should more clearly reflect that investments are needed both on national and global levels. On a national level the recommendations should call for Member States to step up their domestic funding efforts for the implementation of National Action Plans. On a global level the recommendations should call for securing finance of the functions required for the global coordination of the response to AMR. Recommendation E4 should also make a clearer call for financing of new international instruments.
 - 2. Given the push for an increased mandate for the Tripartite, the recommendations should also call for increased funding for the Tripartite. An increased funding commitment by Member States toward the agencies is needed to support capacity-building and enable technical assistance from the Tripartite to countries. Clear milestones and evaluation strategies should also be established to measure the progress of the Tripartite. If the Tripartite falls short, a larger UN response should be triggered.
 - 3. The proposed governance structure in Recommendation E1, the One Health Global Leadership Group, should more clearly meet the functions needed on a global level. Global governance must facilitate national work and allow financing mechanisms to function properly.

- a. We reaffirm the mention of the Committee on World Food Security (CFS) as a model governance mechanism. The responsibility and decision power of Member States must be emphasized in the proposal for global governance.
- b. SUN is not a good model for governance, as its current structure allows for a lot of industry interference.
- c. There is a need to better clarify the roles, mandates and functions of the different stakeholders involved in the multi-stakeholder partnership platform.
- 4. Conflicts of interest need to be avoided in all governance structures and multi-stakeholder engagements. The consideration should bring clarity on how to avoid and if not possible, manage conflict of interests in all governance structures and multi-stakeholder engagements.
 - a. The Independent Panel on Evidence for Action should be truly independent in order to produce sound evidence that can be used as a basis for action, as successfully modeled by the Intergovernmental Panel on Climate Change. Hosting, staffing and funding of the Panel should also be independent to ensure outcomes are not influenced by stakeholders with vested interest and to avoid conflicts of interest.
 - b. The risks surrounding the involvement of the pharmaceutical industry in AMR governance efforts, as covered in Recommendations C2 and D2, should be raised in the recommendations. These include the following:
 - i. Companies have conflicts of interest in marketing their products and promoting prudent use and stewardship
 - ii. Industry can take advantage of a weaker system and lack of resources at the country level to push their influence through access programs, donations or product monopolies.
 - iii. Pharmaceutical industries can use the issue of substandard and falsified medicines to question the quality of generic drugs and unfairly hinder competition. The efforts to remove substandard drugs should be the responsibility of regulatory agencies, independent of industry influence to avoid conflict of interest.
- 5. To ensure accountability and emphasize the need for policy coherence, there should be a clearer call for the IACG recommendations to be considered in the Global Development and Stewardship Framework in Recommendation E4. It will also be important to create indicators to link AMR with the SDGs and clearly recognize that without tackling AMR SDGs will not be possible.
- 6. The process for recommendation implementation needs to be made clearer using a systems and process approach. The principles at the beginning of the report say the recommendations should be practical to implement but do not specify who is responsible for implementing them. There should be a clear mandate as to how and who will implement the recommendations.



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February 19, 2019

To the Interagency Coordination Group on Antimicrobial Resistance:

The Association for Professionals in Infection Control and Epidemiology (APIC) commends the Interagency Coordination Group on Antimicrobial Resistance and supports its draft recommendations to the United Nations General Assembly. APIC is an international nonprofit multidisciplinary organization representing almost 16,000 infection preventionists whose mission is to create a safer world through prevention of infection.

In 2014, APIC joined 24 other health organizations and the U.S. Centers for Disease Control and Prevention (CDC) in a joint statement on antibiotic resistance. As part of this coalition effort, we committed to following principles, which are consistent with the IACG recommendations, to both conserve and replenish our antibiotic resources. APIC members have a primary role in efforts to slow the emergence of resistant bacteria and prevent the spread of resistant infections. Among activities essential to achieving this goal are healthcare policies and antibiotic stewardship programs that improve patient outcomes, and efforts to minimize the development of resistance by ensuring that each patient receives the right antibiotic at the right time at the right dose for the right duration.

APIC has placed high priority on activities to promote antibiotic stewardship, including:

- Advocating for requirements for antibiotic stewardship programs in U.S. healthcare facilities;
- Supporting use of CDC's antibiotic use and resistance surveillance system;
- Educating healthcare facilities, policymakers, scientific experts, and consumers to help them better understand antibiotic use and resistance through online and live educational programs and resources;
- Supporting and promoting recommendations from the U.S. Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) and the U.S. National Action Plan on Combating Antibiotic-Resistant Bacteria.
- Working with stakeholder groups to support reduction of use of antibiotics in the animal agriculture industry; and
- Supporting incentives for development of new antibiotics.

Although APIC's efforts have been primarily U.S.-based, we welcome the opportunity to join with colleagues and other stakeholders around the world to ensure that antibiotics do not turn from a miracle life-saving tool to becoming both ineffective and harmful.

APIC again thanks the IACG for its comprehensive efforts and recommendations to address antimicrobial resistance and we look forward to continuing to work with the WHO to protection public health worldwide.

Sincerely,

Karen K. Hoffmann, RN, MS, CIC, FSHEA, FAPIC

2019 President

Farnt Hoffmann

Association for Professionals in Infection Control and Epidemiology

British Society for Antimicrobial Chemotherapy (BSAC)



United Nations Interagency Coordination Group (IACG) on Antimicrobial Resistance

BSAC response to draft recommendations

Comment number	Section within the Document	Page number	Line number	Comments Insert each comment in a new row.
		Or 'general' for comments on whole document	Or <u>'general'</u> for comments on whole document	Do not paste other tables into this table - type directly into this table.
1		2	General	Disappointing that vaccines are not given greater prominence in the document. In the fight against AMR, vaccines have some unique advantages, and therefore more effective use of existing vaccines and the development of new, effective, vaccines could have a huge impact on AMR. Vaccines already play a critical role, with an impressive track-record of reducing AMR 2. Both <i>H. influenzae</i> b (Hib) and pneumococcal conjugate vaccines (PCVs) have resulted in a dramatic reduction in disease burden and have been associated with decreased incidence of resistant strains. Additionally, both vaccines have an additional "indirect" effect on AMR by reducing antibiotic usage and therefore selection pressure on pathogens. Evidence shows that universal coverage with PCV13 vaccination could avoid 11.4 million days of antibiotic use per year in children under five. In addition to existing vaccines (influenza, Hib, PCVs) there are several new vaccines under development that will have a marked impact on AMR (e.g. vaccines for Cl. difficile, RSV).
2	Section B2	8	General	There is no proper discussion of the value of vaccines. There have been several comprehensive documents that emphasise the value of vaccines as a tool to tackle AMR (e.g. Vaccines and alternative approaches: reducing our dependence on antimicrobials J. O'Neill (https://amr-review.org/sites/default/files/Vaccines%20and%20alternatives v4 LR.pdf); Vaccines for AMR Boston Consulting Group https://www.amr-insights.eu/vaccines-to-tackle-drug-resistant-infections/)
3	Section Accelerate progress in countries	4	General	Recommendation A1 and page 4 on supporting considerations are to be applauded but do not go far enough. Without greater transparency in the whole supply chain, it will not be known if there is sufficient manufacturing resilience to cope with disruption in the many points in the supply chain. There needs to be sufficient API manufacturers to cope with major disruptions alongside greater stockholding for smaller disruptions.
4	Section Accelerate progress in countries	General	General	A2. There needs to be a single top-level measurement for antimicrobial consumption, rather than looking at these separately. This can happen further down. Without this, we will never achieve a true One Health approach. An antibiotic footprint at a country and individual level, similar to a carbon footprint, will help nations and citizens to play their part in reducing their footprint. See www.antibioticfootprint.net as an example.
5	Innovate for the future	General	General	B2. There needs to be easier access to existing antimicrobials across the globe. A review of the licensing arrangements includes fees for older antibiotics needs to be addressed to allow more equitable access to existing antimicrobials.
6	Collaborate for more effective action.	General	General	C1. We support the approach recommended, but this will rely on acceptance that not all funding to improve effective action will come from state funded sources and that collaboration with the private sector can often lead



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BSAC response to draft recommendations

				to greater success.	
7	Collaborate for more effective action.	General	General	C2. The inclusion of environmental contamination into a single global antibiotic footprint would assist the One Health approach by highlighting at a country level the consumption (including contamination).	
8	Collaborate for more effective action.	General	General	C2. Making available existing stewardship resources in multiple languages, tailored to local culture, and free at the point of delivery will help to support stewardship in less affluent countries. Examples, such as the AMS MOOC and AMS e-book from www.bsac.org.uk exist.	
9	Recommendation A1			This is a very laudable recommendation that clearly requires cooperation between the various agencies responsible for the various different areas mentioned. It also requires agreement from national governments to move this forward. Last point in terms of strengthening national surveillance, regulatory and accountability mechanisms, requires a significant investment not least in terms of coordinating data capture, sharing, management, reporting, and interpretation.	
10	Recommendation A2			This recommendation clearly requires establishing a dedicated staff globally and at national level. Main concern would be this may end up being yet another level of bureaucracy rather than an efficient means of achieving the objectives. There is clearly a role diagnostic and pharmaceutical companies to become involved, but their very nature may well prevent them because of the competing interests of shareholders versus stakeholders.	
11	Recommendation A3			Alternatives to using antimicrobials for growth promotion do exist but much more needs to be done and there is no mention of how the necessary finance can be secured.	
12	Recommendation B1			The financial incentives mentioned would require a different approach to rewarding investment than is now the case. Given the experience of the US withdrawing from the climate change agreements and the fact that most pharmaceutical companies are based in that country does not auger well	
13	Recommendation B2			Promoting and supporting equitable and affordable access to existing and new antimicrobial diagnostics vaccines et cetera is a laudable objective but it is not at all clear how this could be achieved without the nations of the world coming together to find common ground.	
14	Recommendation B3			To achieve this the whole notion of protecting intellectual property particularly patents would have to be re- examined	
16	Recommendation D1 & D2			The question arises again on how innovation will be rewarded since the vast majority never see the light of day because of lack of investments, distorted markets, and the like.	



United Nations Interagency Coordination Group (IACG) on Antimicrobial Resistance

BSAC response to draft recommendations

17	Recommendation E1	Agree wholeheartedly this recommendation with the proviso that the group is given a clear mandate and sufficient support to achieve its objectives without becoming bloated bureaucracy
18	Recommendation E2	This seems very sensible but such reports really must be kept as concise and is clear as possible to ensure maximum dissemination not only to politicians, scientists, and other professionals, but as important, to the public at large
19	Recommendation E3	Wholeheartedly support this recommendation but it will stand or fall on the amount of funding allocated to each of the activities mentioned as we know from experience much of what is being done to guide support monitor and evaluate implementation is being done on an ad hoc basis by enthusiastic people who have to find funding from multiple sources other than those provided by government agencies
20	Recommendation E4	with all the urgent matters member states have to deal with individually and collectively it would be good to set a time for achieving this.

Center for Genetic Engineering and Biotechnology of Cuba

Propuesta para mitigar la resistencia a Antimicrobianos:

Título de la presentación: Alternativas al uso de antimicrobianos convencionales. Propuestas del CIGB.

Introducción:

El uso en muchas ocasiones indiscriminado y descontrolado de antibióticos (antimicrobianos) ha ido generando resistencia a los mismos, lo cual constituye un creciente riesgo, no sólo para la Sanidad Animal, también lo es para la Salud Humana.

"Súper-bacterias" así describe este fenómeno de forma sintética y magistralmente la Dra. Monique Éloit, Directora General de la Organización Mundial de Sanidad Animal (OIE) en su alocución en el 71° Período de Sesiones de la Asamblea General de las Naciones Unidas, durante la REUNIÓN DE ALTO NIVEL SOBRE LA RESISTENCIA A LOS ANTIMICROBIANOS el 21 de septiembre de 2016. En esa ocasión también se refirió al "Plan de acción mundial de la OMS sobre la resistencia a los antimicrobianos" (http://apps.who.int/iris/bitstream/10665/249548/1/9789242509762-fre.pdf).

Ningún país, organización regional o mundial, institución estatal o privada, compañía productora de fármacos, etc... puede mantenerse al margen de esta situación, es por ello que debemos poner en función de este problema todas nuestras capacidades y herramientas.

El Centro de Ingeniería Genética y Biotecnología (CIGB) de Cuba (http://www.cigb.edu.cu), aunque tiene como objetivo fundamental la investigación en el área biomédica con el desarrollo y producción de novedosos medicamentos de alto impacto en la salud humana, también cuenta con una dirección de Investigaciones Agropecuarias.

Las Investigaciones Agropecuarias en el CIGB responden a las necesidades de Cuba de aumentar la producción agrícola y ganadera para la satisfacción sostenible de las demandas alimentarias de nuestra población y disminuir la importación de alimentos a la que el país dedica más de 2000 millones de USD anuales. Nuestros proyectos de investigación están dirigidos a la obtención de vacunas y fármacos veterinarios así como a la obtención de bio-productos y cultivos mejorados aplicables a la agricultura industrial y los cultivos intensivos basados en la plataforma biotecnológica creada en el CIGB. En el uso de la ingeniería genética y la biología molecular como métodos de trabajo, estamos completamente conscientes de nuestra responsabilidad para la seguridad humana y la protección del medio ambiente. Con la visión de una sola salud, vemos a la ingeniería genética como método esencial para el desarrollo de nuevos productos y solución de problemas de la ciencia y la tecnología en la esfera agropecuaria. Nuestro trabajo está dirigido hacia esos objetivos sobre valores éticos, llevando a cabo los mismos con una evaluación de los riesgos y siguiendo las más estrictas medidas de bioseguridad de acuerdo con los requerimientos exigidos por las legislaciones vigentes.

Desarrollo:

A continuación, listamos los proyectos fundamentales (en ejecución) del CIGB en sus etapas de desarrollo. En la tabla aparecen con fondo amarillo los que se vinculan de forma directa con la sustitución y/o el uso adecuado de los antimicrobianos en sentido general:

PROYECTOS DE BIOTECNOLOGIA AGROPECUARIA DEL CIGB

PROYECTO	ÁREA	INVESTIGACIÓN	DESARROLLO A ESCALA PILOTO	ENSAYOS DE CAMPO	REGISTRO
GAVAC: IMNONOGENO PARA EL CONTROL BIOLOGICO DE LAS GARRAPATAS DEL GANADO BOVINO	VETERINARIA				
HeberNEM: BIONEMATICIDA ECOLOGICO Y ESTIMULADOR DEL CRECIMIENTO DE LAS PLANTAS.	AGRICULTURA				
Porvac: Vacuna de Subunidad Contra la Peste Porcina Clásica (PPC).	VETERINARIA				
KestoZyme: BIOCATALIZADOR PARA LA PRODUCCIÓN DE FRUCTOOLIGOSACÁRIDOS (FOS: prebiótico) A PARTIR DE SACAROSA.	ENZIMAS INDUSTRIALES				
ACUABIO 4: SUPLEMENTO NUTRICIONAL, ESTIMULADOR DEL CRECIMIENTO Y EL SISTEMA INMUNE EN ORGANISMOS ACUÁTICOS.	ACUICULTURA				
CIGBL1, L7 y RP5: PLANTAS DE SOYA TRANGENICAS A GLIFOSATO.	AGRICULTURA				
CIGB -552vet: CITOSTATICO BIOLOGICO PARA EL TRATAMIENTO DEL CÁNCER EN ANIMALES DE COMPAÑIA.	VETERINARIA				
PLANTAS DE SOYA TRANGENICA CON EL GEN DE LA DEFENSINA PARA COMBATIR ENFERMEDADES FUNGOSAS.	AGRICULTURA				
CunVac: VACUNA RECOMBINANTE CONTRA LA ENFERMEDAD HEMORRAGICA DEL CONEJO	VETERINARIA				
ACUABIO V: ESTIMULADOR DEL SISTEMA INMUNE Y EL CRECIMIENTO EN LOS ORGANISMOS ACUATICOS	ACUICULTURA				
SalVac: CANDIDATO VACUNAL CONTRA EL PIOJO DE MAR, ECTOPARASITO DE LOS SALMÓNIDOS.	ACUICULTURA				
Sistemas de diagnóstico rápido: Inmunoensayos "HeberFast Line"	VETERINARIA				
VACUNA PO: CANDIDATO VACUNAL CONTRA GARRAPATAS BASADA EN LA PROTEINA PO.	VETERINARIA				
CIGB 42: PARA EL CONTROL DE ENFERMEDADES INFECCIOSAS EN PLANTAS.	AGRICULTURA				
OBTENCIÓN Y DESARROLLO DE LA DEXTRANASA	ENZIMAS INDUSTRIALES				
VACUNA PARA LA INMUNOCASTRACIÓN BIOLOGICA	VETERINARIA				
PÉPTIDOS ANTIMICROBIANOS	VTERINARIA				

A continuación se detallan los proyectos (productos) vinculados al tema:

KestoZyme: Biocatalizador para la producción de fructooligosacáridos (FOS) a partir de sacarosa					
	Área Agrícola: Plataforma Tecnológica				
OBJETIVO	Explotación comercial de una tecnología novedosa para la producción de FOS de alta calidad a partir de azúcar de caña o azúcar de remolacha.				
DESCRIPCIÓN	Los fructooligosacáridos comerciales (comúnmente denominados FOS) son azúcares no digeribles, derivados de la sacarosa, constituidos por varias unidades de fructosa y una glucosa terminal. Los FOS son prebióticos de creciente demanda en el mercado de los alimentos funcionales. La ingestión de FOS promueve la proliferación selectiva de bífidobacterias y lactobacilos, principales representantes beneficiosos de la microflora intestinal de animales y humanos. Este efecto está asociado a importantes beneficios para la salud, tales como: exclusión competitiva de patógenos intestinales, reducción del colesterol sérico, incremento en la absorción de calcio y magnesio, prevención del cáncer de colón, y producción de vitaminas del tipo B. El trisacárido 1-kestosa (GF ₂) es el FOS de mayor interés comercial debido a su rápido efecto prebiótico y su aún sabor dulce.				
	fructosiltransferasa (1-SST) de origen vegetalque se puede operar de forma estable, ya sea en procesos repetitivos, en batch o en columnas a flujo continuo.				
	En ambos sistemas, el sustrato sacarosa se transforma esencialmente en glucosa FOS de cadenas cortas. Durante la reacción, el contenido de FOS alcanza el 60% d los carbohidratos totales y la 1-kestosa representa el 90% de los FOS producidos.				
PATENTE	La tecnología de producción de FOS a partir de utilización de la fructosiltransferasa en procesos con bioreactores de membrana se encuentra protegida por la patente "Método de obtención de 1-kestosa". Nro de solicitud en Cuba: CU2012-0138. Presentada a la OCPI: septiembre 2012.				
ESTADO DEL PROYECTO	 Tecnología de producción de enzima 1-SST pura, liofilizada y estable. Tecnología para producción y operación de biocatalizador desarrollada hasta escala piloto. 				
TIPO DE COLABORACIÓN SOLICITADA	Alianza estratégica y asociación para: • Partners para comercialización de enzima 1-SST				
VENTAJAS COMPETITIVAS E HITOS	El biocatalizador desarrollado en el CIGB es más competitivo que los sistemas productivos actuales, basados en el uso de hongos filamentosos, en términos de: • Mayor rendimiento y calidad de FOS (90% 1-kestosa y 10% nistosa) • Escasa actividad de hidrólisis de sacarosa • Bajo costo de producción y operación simple.				
	Código del proyecto: AGBIO/CIGB/2014-03				

Acuabio 4, un potente	inmuno-estimulador y suplemento nutricional para organismos acuáticos
	Área Agrícola: Acuicultura
OBJETIVO	Acuabio 4 es una formulación que puede utilizarse como aditivo de piensos para peces, estimula el crecimiento y la calidad de las larvas en especies acuícolas. Ha demostrado mejorar la sobrevida, los parámetros inmunes innatos y adaptativos, el apetito y la resistencia a las infecciones por patógenos.
DESCRIPCIÓN	El CIGB ha descubierto y está desarrollando una formulación, denominada Acuabio 4, que mejora el crecimiento, la sobrevida, los parámetros inmunes innatos y adaptativos, el apetito, la resistencia a las infecciones por patógenos en organismos acuáticos y la respuesta a tratamientos antivirales, ya sea como formulación adicionada a piensos para peces y crustáceos por vía parenteral, como parte de una composición antiviral o de una terapia veterinaria combinada. Los resultados han sido ya probados en Cuba a escala controlada.
	Este producto es un péptido activador de la adenilato ciclasa de la pituitaria, que estimula la liberación de la hormona de crecimiento. Esta es una tecnología no mediada por transgénesis.
	Al ser probado en pez gato, tilapia, carpa y camarón, Acuabio 4 generó:
	 Crecimiento en corto tiempo. Incremento de la sobrevida. Estimulación del sistema inmune innato y adaptativo. Estimulación del apetito. Resistencia a la infección por patógenos. Su evaluación in vivo contra virus (IPNV, el VHSV, ISAV, WSSV, YHV, TSV, IHNNV y MBV) que afectan a salmónidos, camarones peneidos, y bivalvos, demostró una respuesta sinérgica cuando fue combinada con antivirales, en comparación con los grupos tratados con el antiviral o el péptido solo, en cuanto a reducción de la carga viral e incremento de la sobrevida.
ESTADO DE	WO 2007059714 A1. Neuropeptides for the culture of aquatic organisms.
PATENTE	WO/2012/072055 A1. Use of pacap for treating viral infections in aquatic organisms.
	WO 2013029570 A1. Use of the pacap as a molecular adjuvant for vaccines.
ESTADO DEL PROYECTO	Se tiene una formulación final para adicionar al pienso animal y una formulación como adyuvante molecular de vacunas de peces.
TIPO DE	Establecer Acuerdos de Evaluación para demostrar las potencialidades del Acuabio 4.
COLABORACIÓN SOLICITADA	Acuerdos de desarrollo de producto final y evaluación, vinculados a una estructura de pagos por hitos vencidos.
	Acuerdos comerciales para territorios específicos.
VENTAJAS COMPETITIVAS e HITOS	Acuabio 4 ha demostrado capacidad de mejorar el sistema inmune innato y adaptativo, con un incremento en la sobrevida, reducir el ciclo de desarrollo del pez, con una mayor ganancia de peso en el tiempo. Se ha demostrado una mejor respuesta a las vacunas de peces
	Código del proyecto: AGBIO/CIGB/2014-04

PÉPTIDOS ANTIMICROBIANOS				
	Área: Veterinaria			
OBJETIVO	Obtener un nuevo producto con Propiedad Intelectual, que podría ser empleado como un antimicrobiano de nueva generación o como adyuvante molecular.			
DESCRIPCION	Este es un proyecto de investigación aplicada, dirigido a obtener un nuevo producto con Propiedad Intelectual. Los candidatos obtenidos en el mismo pudieran ser empleados fundamentalmente como antimicrobianos de nueva generación para la prevención y/o tratamiento de enfermedades infecciosas. Pudieran ser utilizados, además, como adyuvantes moleculares. Acuabio 6, nuevo candidato antimicrobiano y potencial inmunoestimulador, abarca tres péptidos antimicrobianos: Oreochromicina-1, Oreochromicina-2 y Oreochromicina-3, relacionados con péptidos de la familia de la dicentracina, la moronecidina y la pleurocidina, respectivamente.			
SITUACIÓN DE PATENTE	El espectro antimicrobiano de estas moléculas y su propiedad como adyuvantes moleculares se incluyen en una patente presentada y publicada entre 2011 y 2013 (Secuencias de aminoácidos para el control de patógenos. PCT/CU2012/000005. WO 2013/044890 A1). Concedida en Cuba, Europa, Estados Unidos, Japón, Australia y China. En fase nacional en otros países.			
FASE DE DESARROLLO CONCLUIDA Y ESTADO DEL PROYECTO	En fase de investigación.			
TIPO DE COLABORACIÓN SOLICITADA	Asociación corporativa para licencia, co-desarrollo y comercialización.			
	Código del Proyecto: AGBIO/CIGB/2016-07			

En el caso de los Sistemas de diagnóstico rápido (Inmunoensayos "HeberFast Line") pueden ser una herramienta que permitirá precisar el uso de los antimicrobianos ante diversas sintomatologías que aparentemente pueden ser debidas a una patología a la que no le correpondería el uso de determinado antibiótico.

A continuación ejemplificamos con uno de los sistemas de diagnóstico rápido que se ha desarrollado en el CIGB, que aunque no tenga relación directa con el tema de la resistencia a antimicrobianos, sí puede ser un modelo o prototipo de lo que pudiera desarrollarse para el diagnóstico rápido y preciso de patologías que pudieran requerir (o nó) un antimicrobiano determinado:

Desarrollo de un	sistema rápido de diagnóstico de Peste Porcina Clásica (E2-PPC)
	Área Agrícola: Diagnóstico
OBJETIVO	Desarrollo de un sistema de diagnóstico rápido de proteína E2 de Peste Porcina Clásica, como parte de una aproximación integral al control y erradicación de esta enfermedad.
DESCRIPCIÓN	La Peste Porcina Clásica es una enfermedad viral altamente contagiosa, clasificada dentro de la lista de enfermedades de declaración obligatoria de la Oficina Internacional de Epizootias (OIE). En la actualidad las exigencias por desarrollar inmunoensayos rápidos y sencillos para el diagnóstico humano y veterinario se han incrementado. La rapidez y versatilidad de diferentes sistemas diagnósticos presentan algunas ventajas, incluyendo sensibilidad, simplicidad y bajo costo, todo lo cual repercute significativamente en materia del resultado a obtener (Foy, 2003). En el CIGB se ha desarrollado un ensayo rápido, visual y cualitativo, de tipo inmunocromatográfico (tiras reactivas), para determinar los anticuerpos específicos contra la proteína E2 del VPPC en muestras de suero porcino, que correlaciona con la técnica de seroneutralización utilizada tradicionalmente y con el ELISA comercial Ceditest CSFV Ab.
ESTADO DE PATENTES	Know How específico.
ESTADO DEL PROJECTO	Registro sanitario solicitado en Cuba. Un sistema DIVA se encuentra en desarrollo, para la diferenciación de animales vacunados con vacuna de subunidad, de los infectados.
TIPO DE COLABORACIÓN SOLICITADA	Establecer acuerdos de Desarrollo y Evaluación para efectuar ensayos que permitan comprobar las potencialidades del sistema de diagnóstico rápido de proteína E2 del VPPC (tiras reactivas).
COLIGITADA	Identificación de las contrapartes apropiadas para extender su uso y aplicación.
	Los acuerdos que se establezcan para la evaluación estarán ligados y vinculados a una estructura de pagos por adelantado y por hitos obtenidos.
	Los resultados obtenidos darán lugar al establecimiento de acuerdos comerciales posteriores para territorios específicos y por un plazo de tiempo determinado.
VENTAJAS COMPETITIVAS E HITOS	Evaluado con varios paneles de muestras de suero previamente certificadas por el ensayo NPLA del CENSA, así como con paneles de muestras del Laboratorio de Referencia Europeo EURL (European Union Reference Laboratory) radicado en Hannover, Alemania. Aún cuando los sistemas evaluados no tienen el mismo principio, las tiras reactivas reportan niveles de sensibilidad del 96.01 % y especificidad del 97,65 % frente al NPLA como prueba que mide la respuesta de anticuerpos neutralizantes. Herramienta útil para control de circulación viral en regiones donde esté prohibida la vacunación y de efectividad de inmunización, donde se utilice este método como parte del control de la enfermedad.
	Project code: AGBIO/CIGB/2014-06

Conclusiones:

- 1. La Ingeniería Genética y la Biotecnología constituyen herramientas que con un financiamiento adecuado, pueden ser usadas para disminuir la aparición de resistencia a antimicrobianos
- 2. El CIGB pone a disposición de la Sanidad Animal, específicamente en el objetivo de mitigar el fenómeno de la resistencia a antimicrobianos, los recursos y líneas de trabajo con que cuenta.

DRAFT RECOMMENDATIONS OF THE AD-HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE

Comments from the Centre for Science and Environment (CSE), India

Res	pon	den	ts:

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1. Recommendation A1

1.1 Recommendation A1, subsection e: "Development of national instruments based on international standards for equitable access to and prudent use of existing and new quality-assured antimicrobials in humans, animals, plants and food production, as well as waste management in health care, manufacturing and farming-related activities."

CSE comment:

This subsection calls for development of national measures based on international standards for waste management in health care, manufacturing and farming-related activities. While waste management could comprise of several procedural approaches such as better composting, better waste disposal, setting up of an effluent treatment plant etc., it does not address how the efficiency of waste management could be measured or what should be the yardstick to conclude that waste has been managed appropriately in view of antimicrobial resistance (AMR) containment. In this regard, it is important that country governments develop environmental standards for residual antibiotics in waste from different point sources such as food animal production settings; slaughter houses; fish, meat, dairy processing units; human and veterinary healthcare settings; feed manufacturing units; pharmaceutical manufacturing units etc. Unless regulatory standards are set, waste management will not be binding on any entity generating waste. It is also important to note that there are presently no international examples or global best practices linked to standards for residual antibiotics in the environment. However, this should not be a reason for slow/no progress of countries (such as India or China who are bulk producers of antibiotics) on this front. Necessary global as well as consumer pressure for relevant laws to aid in successful waste management must be created.

In addition, emphasis must be given to "pharmaceutical manufacturing" in Recommendation A1, subsection e, since they are one of the key sources of residual antibiotics in the environment.

1.2 Recommendation A1, consideration section: "The IACG recognizes that effective systems for infection prevention and control, including clean water, sanitation and hygiene, and Good Management Practices and biosecurity in farming, avert infections associated with health care and farming-related activities. This will protect patients, health and farm workers, as well as animals and plants, thereby reducing the future need for antimicrobials, preserving the environment and ensuring sustainable food production. Furthermore, proper management and handling of soil, water, health facility and pharmaceutical waste, as well as manure used as fertilizer, can further reduce the spread of antimicrobial residues along the food production chain and in the environment."

CSE comment:

Management of waste and appropriate handling of soil, water etc. will not only reduce the spread of antimicrobial residues along the food production chain and in the environment, but will also limit the spread of other determinants of resistance such as resistant bacteria. It is recommended that incorporation of this aspect in the text is considered.

1.3 Recommendation A1, consideration section: "Effective national-level antibiotic demand forecasts: These are needed in both human and animal health to improve access to antibiotics and to strengthen procurement and supply chain management. This will in turn support efforts by WHO and OIE to develop a global demand forecast model for antibiotics that can be shared with manufacturers on a regular basis and made publicly available."

CSE comment:

The above statement could be interpreted in a way that potentially favours more antibiotic use in animals. Limited access to antibiotics in case of animals could be true for a particular antibiotic or a particular disease outbreak caused by a bacterial infection. However, this should not be generalized to reflect that there is an overall access issue with antibiotics in case of animals, as is being reflected in the text here. In an attempt to create a global demand forecast, the larger and important objective of reducing antibiotic misuse in animals to contain emergence and spread of AMR will remain unaddressed. The net effect on antibiotic stewardship will be adversely impacted. A proper understanding on the access issue of antibiotics in case of animals is thus required. Moreover, access and excess to antibiotics are two different issues. In the event of no targets to reduce misuse and overall use, the gap in access is more likely to reduce than excess, whereas ideally both of these should be handled separately. In view of the above, it is suggested that the language for this text be reconsidered to avoid misinterpretation.

1.4 Recommendation A1, consideration section: "The prudent use of antimicrobials across human, animal, plant and environmental sectors requires appropriate attention to and investment in training, accreditation and regulation of professionals, including physicians, pharmacists, veterinarians and other specialists across human, terrestrial and aquatic animal and plant health, as well as in food production and the environment. The IACG recognizes that in many settings, non-physicians (such as nurses, paramedics and community health workers) and veterinary paraprofessionals may also be trained and authorized to prescribe or administer some antimicrobial agents."

CSE comment:

It is suggested that some text may be considered for addition after this text, which highlights that capacity building of non-physicians should be carefully done as well as monitored to avoid excess antibiotic prescription, administration or their misuse.

1.5 Recommendation A1, consideration section: "The IACG emphasizes that there is an urgent need to strengthen regulatory frameworks and enforcement capacity in all countries to enable effective national responses to antimicrobial resistance, including on the prudent use of antimicrobials to regulate the sale of antimicrobials particularly antibiotics over the counter or through the internet."

CSE comment:

The IACG mentions the urgent need to strengthen regulatory frameworks and enforcement capacity of over the counter as well as online sale of antimicrobials. In addition to these, import of antimicrobials is also another area of concern. Imported antibiotics are not regulated in countries belonging to the low and middle income group, thereby leaving scope for entry of spurious or substandard antibiotics in the country. It is strongly recommended that antibiotic import is also considered as an area that requires regulatory intervention. Further, it will also be useful to introduce onus and responsibility on drug manufacturers, such as through drug/antibiotic take-back programmes along the lines of extended producer responsibility.

2. Recommendation A2:

"The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs,"

CSE comment:

While the narrative linking National Antimicrobial Resistance Action Plans and SDGs is quite strong, it would still be useful to have greater clarity in terms of how to go about it i.e. actions required by nations, tripartite along with the United Nations Environment Programme etc. Presently, the consideration section under Recommendation A2 does not mention much of this.

3. Recommendation A3

"The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins)".

CSE comments:

• While the background section in the draft IACG recommendations recognises the role of routine use of antimicrobials in development and spread of AMR in both animals and humans, recommendation A3 provides for a weak action on growth promoter use. In reality, there is a very thin line between growth promoting effect and disease preventative effect when an antibiotic is being administered at low or sub-optimal doses for longer duration of time. Recommendation A3 does not address the other aspect of non-therapeutic use (i.e. disease prevention), which is also routine and can further increase if growth promoter use is restricted. It is strongly recommended that the disease prevention aspect is given equal importance and addressed.

 The recommendation specifically outlines that growth promoter phase out should begin immediately with the Highest Priority critically Important Antimicrobials (HPCIAs). It therefore indicates that HPCIAs should not be used for growth promotion.

HPCIAs are the most important category of antimicrobials within the CIAs, which should be preserved for human use and not be encouraged for use in animals at all, be it disease treatment, disease prevention or growth promotion. The WHO guidelines on use of medically important antimicrobials in food-producing animals, released in 2017, clearly mentions that CIAs should not be used for control of the dissemination of a clinically diagnosed infectious disease identified within a group of food-producing animals, and HPCIAs should not be used for even treatment of food-producing animals.

In this context, Recommendation A3 should therefore not emphasize on the need to phase out on HPCIAs specifically in case of growth promotion.

• The main text of the recommendation outlines the phase out of antimicrobials for growth promotion consistent with guidance from the tripartite, thereby leading to incoherence. While on one hand, the WHO guidelines on use of medically important antimicrobials in food-producing animals, clearly indicates no such use, there is reference to risk analysis as per OIE codes in the consideration section of the Recommendation, which would make the phase out very difficult, at least in the short-term.

The OIE guidelines on risk analysis are scientifically very demanding and are designed to be elaborate, long-term and cost-prohibitive. For a resource and capacity constrained LMIC, this is going to be a challenging task. It is unlikely that the country will be able to execute such risk assessments within a stipulated time. This will also allow governments to delay action citing need for more evidence, which in turn will again depend on several factors such as availability of financial resources to fund research studies, industry influence etc. Overall, recommending phase out of growth promoting antimicrobials based on risk analysis will be a regressive step that will impede the growing global momentum on addressing growth promoter use in animals.

Recommendation A3 also does not address the need for overall reduction of antimicrobials in food-animal production, or the relevance of setting targets by countries in order to reduce overall antimicrobial use. Setting of targets is one of the most important indicators that measure a country's progress w.r.t. monitoring antimicrobial use in human as well as veterinary sector. The absence of appropriate base-line information as well as country level targets will negatively impact surveillance of antimicrobial use, understanding on linkages with resistance trends and subsequent policy decisions. It is suggested that the relevance of overall reduction of antimicrobial use in food-animal and need for. Setting country-level targets is highlighted in this recommendation.

Consumer Reports



Comments of Consumer Reports on Draft Recommendations of the Ad Hoc Interagency Coordination Group on Antimicrobial Resistance

February 15, 2019

Consumer Reports welcomes the opportunity to comment on the Draft Recommendations of the Ad Hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance. Antimicrobial resistance is a growing global problem that threatens human health in the United States and throughout the world. We commend the IACG for developing these extensive recommendations for practical action, and for opening them for public comment, before transmitting them to the UN Secretary General later this year.

Consumer Reports is an independent U.S. non-profit organization that works side by side with consumers for truth, transparency and fairness in the marketplace, through research, testing, journalism and advocacy.² We have more than 6 million members, and more than 1.5 million volunteers and online activists. Consumer Reports seeks to establish strong pro-consumer policies and protections.

Established more than 80 years ago, Consumer Reports is a founding member of Consumers International, which now has more than 200 member organizations in more than 100 countries. Consumer Reports has represented Consumers International in various fora on the issue of antibiotic resistance and how to address it.

Consumer Reports shares the IACG's commitment to addressing this issue. Over the past several years, we have published numerous articles on antimicrobial resistance in our flagship magazine to provide consumers with actionable information;³ we have lobbied state and federal legislative and regulatory bodies to adopt policies to reduce antibiotic use; and have partnered with other organizations to achieve changes in corporate practice regarding food animal production through marketplace action.⁴

The IACG has developed an important set of recommendations in a number of areas. We are especially interested in those related to animal agriculture. We submit our comments and suggestions below on the recommendations of concern to us.

¹ O'Neill J (Chair). 2016. Tackling Drug-Resistant Infections Globally: Final Report and Recommendations The Review on Antimicrobial Resistance. At: https://amr-review.org/sites/default/files/160525 Final%20paper with%20cover.pdf

² www.consumerreports.org

³ https://www.consumerreports.org/health/how-to-stop-the-overuse-of-antibiotics-in-our-food-supply/

⁴ https://www.antibioticsoffthemenu.org/score-cards/

Recommendation A3: The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO) starting with an immediate end to use of the Highest Priority Critically Important Antibiotic Agents (i.e., quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins).

We support this recommendation, since it recognizes the importance of reducing usage of antibiotics in animal agriculture. However, we urge rewording of the recommendation to make it more specific, and explicitly consistent with the guidance from the Tripartite agencies, including WHO's *Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals*. In terms of the main recommendation--to end use of medically important antimicrobials for growth promotion--we note that this is consistent with action taken by a major animal drug manufacturer and the national policies of many Member States, as well as joint advice from the Tripartite agencies that judicious use of antimicrobials means they should only be used to treat or control disease. We also urge the IACG to call out the need for an overall targeted global reduction in usage of antibiotics, especially medically important antibiotics, in food animal and plant food production. Consequently, we suggest the following rewording:

"The IACG calls on Member States to:

- Reduce use of antimicrobials in food animal and plant production with targeted reduction goals and timelines determined by countries' specific conditions.
- End use of medically important antimicrobials for growth promotion purposes immediately.
- End use of medically important antibiotics for disease prevention purposes, except where a veterinary professional judges there is a high risk of spreading a specific infectious disease, based on a recent culture and sensitivity testing results.
- Use antimicrobials to treat or control disease consistent with the guidance of the *Tripartite agencies (FAO, OIE and WHO)*.
- End use of Highest Priority Critically Important Antimicrobials (i.e., quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins) for growth promotion, disease prevention and disease control in food animal or plant production and use only for disease treatment if it is the only treatment option as determined by recent culture and sensitivity testing results."

Rationale for Suggested Rewording

Antimicrobial use in agriculture often exceeds human use, particularly in highincome countries with industrialized farm animal production systems where large numbers of animals are raised together in confined conditions. In the United States, more than half of medically important antibiotics are sold for use in animals.⁵ Such industrialized farm animal production systems often routinely administer antibiotics in subtherapeutic doses in the animal feed. A 2015 study, by an international team of scientists, has estimated that such industrialized farm animal production systems are set to dramatically expand in mid- and low- income countries, particularly Brazil, Russia, India, China and South Africa, leading to an "antimicrobial consumption increase of 99% [by 2030], up to seven times the projected population growth" in these countries.⁶ Antimicrobial use in industrialized agricultural systems will increase antibiotic resistance. Clearly, there is a need to reduce antimicrobial use in food production.

At least one major producer of antibiotics is already moving in this direction. In 2015, Elanco, the second largest supplier of antimicrobial drugs globally, announced that they would not promote the use of shared-class antibiotics for animal growth or feed efficiency and would remove growth promotion label claims from all medically important antimicrobials sold globally. In late 2018, Elanco announced that they had completed this task, removing label claims for growth promotion on almost 100 products globally.

The need to limit antibiotic use in animals is already well recognized in the European Union and the United States, and many other countries. According to the OIE, in 2017, 110 of 155 countries surveyed do not allow use of antimicrobials for growth promotion. An IACG recommendation that all medically important antimicrobials should be prohibited immediately for growth promotion will thus require no change for 71 percent of countries. To protect the effectiveness of antibiotics, IACG should urge the remaining Member States to also enact such restrictions as soon as possible.

Progress is also needed in reducing antibiotic use for disease prevention in animals. Civil society has worked with food retailers to achieve voluntary reductions in food animal antibiotic use for disease prevention. A coalition of six US consumer, environmental and animal welfare groups including Consumer Reports has published the

⁵ https://www.nrdc.org/experts/avinash-kar/livestock-antibiotic-sales-drop-remain-very-high

⁶ Pg. 5649 in van Boeckel TP, Brower C, Gilbert M, Grenfell BT et al. 2015. Global trends in antimicrobial use in food animals. PNAS 112(18): 5649-5654. At: https://www.pnas.org/content/pnas/112/18/5649.full.pdf

 $https://assets.ctfassets.net/f77lgyyxjmq2/4Tvrvy932oIMgOy0q8sgqg/813539917bd277949d5f36f88add26d8/easset_upload_file37598_111948_e.pdf$

⁸ https://www.elanco.com/news/press-releases/elanco-animal-health-expands-commitment-to-fight-antimicrobial-resistance

⁹ World Organization for Animal Health (OIE). 2019. OIE Annual Report on antimicrobial agents intended for use in animals. Third Report. At:

 $http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/AMR/Annual_Report_AMR_3. pdf$

Chain Reaction scorecard for the last four years using the WHO Guidelines as a benchmark. Of the top 25 fast food chains in the US, the number that have policies that conform to the WHO Guidelines on disease prevention has risen from five to eighteen in 2018, for the chicken they serve. Among those with such policies are the three largest *global* fast food chains, and these companies are beginning to extend their policies to the global level.

The majority of antimicrobial use in many industrialized farm animal production systems is for uses in healthy animals not exhibiting signs of infectious disease (e.g., for growth promotion and disease prevention). Given the serious problem of antimicrobial resistance, there is agreement that antimicrobials should only be used to treat or control infectious diseases. A poster on Antimicrobial Resistance jointly put out by the Tripartite agencies (WHO/FAO/OIE) as part of Antibiotic Awareness Week in 2015 states, under "What the Agriculture Sector Can Do: 1) ensure that antibiotics given to animals—including food-producing and companion animals—are only **used to control or treat** infectious diseases and under veterinary supervision" (bold in original).

It is thus appropriate for the IACG to call on Member States to implement the WHO Guidelines specifically.

We have one further concern about the **Considerations for this**recommendation section. The third bullet states: "It is particularly important that all countries employ appropriate risk analysis – the process of hazard identification and risk assessment, management and communication – as described in the OIE Terrestrial Animal and Aquatic Animal Health Codes. Such risk analyses should be unbiased assessments that transparently present the evidence base for findings and recommendations and be subject to peer review." We suggest that this be reworded to make it clear that, while risk analysis should be used when approving antimicrobials, there is no need to do a risk analysis for use of medically important antimicrobials for growth promotion purposes, because such use should not be allowed. As the Tripartite agencies have noted, antimicrobials should only be used to control or treat infectious disease, not for growth promotion or disease prevention. WHO's *Guidelines on Use of Medically-Important Antimicrobials in Food Producing Animals* also clearly states that medically important antimicrobials should never be used for growth promotion.

To clarify the appropriate use of risk analysis, we urge that the IACG revise the third bullet to read, "It is particularly important that all countries employ appropriate risk analysis **when approving antibiotics for animal use...**" (addition in **bold**). The IACG should further add an extra sentence to the above two sentences that reads, "Such risk

¹⁰ https://www.antibioticsoffthemenu.org/score-cards/

¹¹ https://uspirg.org/sites/pirg/files/ChainReaction4_Report-10_17_18.pdf

¹² https://www.who.int/mediacentre/events/2015/world-antibiotic-awareness-week/agriculture-poster.jpg?ua=1

analyses are not appropriate for medically important antimicrobials proposed for growth promotion purposes, because such uses should not be allowed."

Recommendation B2: The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

We support this recommendation, since there is a great need for equitable and affordable access to both present and future antimicrobials and alternatives to antibiotics. However it is important to clarify that the alternatives to antibiotics can be either alternative substances (such as prebiotics, phages, competitive exclusion products, immune modulators, organic acids, etc.) or alternative practices, such as improved sanitation, good animal husbandry practices, appropriate stocking densities for animal agriculture; or crop rotation, integrated pest management practices, and improved soil health for plant agriculture. Thus, we suggest adding an extra sentence to the recommendation that reads, "Such alternatives may include substances (such as prebiotics, phages, or immune modulators) or practices (such as improved sanitation, good animal husbandry practices, integrated pest management, or improved soil health)."

In the **Considerations for this recommendation**, we suggest adding a third bullet which reads, "The IACG recommends greater efforts to disseminate practices for fighting animal diseases, including improved sanitation, prevention of disease, appropriate stocking density and other sound animal husbandry approaches. There should also be greater dissemination of practices to promote plant health and minimize pests and diseases such as crop rotation, integrated pest management practices and improved soil health." The reason for adding this bullet is to make it clear that alternatives to antibiotics can also include practices, since the first two bullets focus on alternative substances.

Recommendation C1: The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels through: ... c. Provision of political, financial and technical support for civil society organizations to enhance their engagement, including for work with governments.

We support this recommendation, since we see through our own work what civil society engagement can accomplish.

The second bullet of **Considerations for this recommendation** notes that "consumer groups have advocated successfully for responsible antibiotic use in food production by some companies, mainly in high-income countries." With financial support, consumer organizations outside of the high income countries could also successfully advocate for such responsible antibiotic use in food production. Thus, we suggest adding an additional sentence in the second bullet: "Providing funding could enable sharing of strategies among consumer and other civil society organizations to bring pressure in the marketplace to increase availability and sales of food from production systems than minimize or eliminate use of antimicrobials, especially medically important antimicrobials."

Recommendation E2: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE, WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.

We strongly support this recommendation as it would provide much needed guidance across intergovernmental agencies on how best to weigh available evidence and to adopt policies to address antimicrobial resistance. The recent experience with colistin illustrates the value of sharing scientific findings and the potential usefulness of a Panel to evaluate new information. Colistin is a last-resort antibiotic able to treat certain otherwise resistant infections. In 2016, a colistin resistance gene, *mcr-1*, was described that appeared on a plasmid in *E. coli* in China. A detailed phylogenetic analysis published in 2018 found the gene likely originated in Chinese livestock around 2006 and, in the next ten years, spread to 31 countries on five continents. The emergence and spread of this mobile colistin resistance gene so quickly throughout the world shows that a global response to new resistance threats is needed, since the emergence in one country can rapidly spread as a result of global trade and travel.

The recommendation would be strengthened by an addition to the fourth bullet of Considerations for this recommendation, which references the need for the proposed Independent Panel to "draw on the experiences and lessons of similar, existing entities." In addition to reference to International Panel on Climate Change, the Joint Expert

¹³ Liu, YY, Wang Y, Walsh TR, Yi LX et al. 2016. Emergence of plasmid-mediated colistin resistance mechanism *mcr-1* in animals and human being in China: a microbiological and molecular biological study. *Lancet Infectious Diseases* 16: 161-168. At:

¹⁴ Wang, R, can Dorp L, Shaw LP, Bradeley P et al. 2018. The global distribution and spread of the mobilized colistin resistance gene *mcr-1*. *Nature Communications*. At: https://www.nature.com/articles/s41467-018-03205-z.pdf

Committee on Food Additives and the Joint Meeting on Microbiological Risk Assessment, we urge inclusion of the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD). This report will also provide useful information to the expert panel. The IAASTD was a global scientific assessment initiated by the World Bank and the United Nations and completed in 2008 to evaluate the state of global agriculture, its history and future and make recommendations for the future of farming. ¹⁵ The IAASTD Global Report and regional reports contain discussion of antimicrobial usage in agriculture and discusses ways to minimize such uses.

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¹⁵ https://www.globalagriculture.org/report-topics/about-the-iaastd-report.html

European & Developing Countries Clinical Trials Partnership (EDCTP)

From: Pandya, Lara
To: IACG-secretariat

Subject: Feedback on the draft recommendations of the IACG on Antimicrobial Resistance

Date: Monday, February 18, 2019 13:28:44

Dear IACG Secretariat,

On behalf of the European & Developing Countries Clinical Trials Partnership (EDCTP), I would like to take the opportunity to comment on the <u>draft recommendations of IACG on Antimicrobial Resistance</u>, which we read with interest. Our comment relates specifically to Section B, recommendation B1 on page 7 of the document. In the fourth bullet of considerations for this recommendation the IACG acknowledges the important and encouraging role of existing international mechanisms to support research and development in human health. However, we note that EDCTP is absent from the list of examples of such existing mechanisms provided.

Akin to the Innovative Medicines Initiative (IMI), EDCTP is a European Union (EU)-related partnership that manages EU funds together with pooled funds from its Participating States and other public and private partners in support of clinical research to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against poverty-related infectious diseases in sub-Saharan Africa. You may have seen that EDCTP featured heavily in the G-FINDER Report 2018, owing to a significant increase in funding in 2017 from the EU and the UK, which reflects the fact that EDCTP is one of the major global funders of research and product development for neglected diseases in developing countries. As at 31 December 2018, through its second programme (EDCTP2, running from 2014-2024), EDCTP has committed € 487.8 million to Research and Innovation Actions - EDCTP2's main financing mechanism for supporting clinical research and product development. EDCTP-funded work to date spans 36 African countries. This work is advancing the development of drugs, vaccines, diagnostics and other interventions that will make a real difference to the lives of people across the continent. Details of these activities are available in a comprehensive EDCTP report on success stories through R&D partnerships to tackle infectious diseases in Africa. Antimicrobial resistance is an overarching theme in the majority of these activities. As one of the EU's flagship programmes, we therefore believe that EDCTP should feature among the list of examples of existing international mechanisms to support research and development in human health.

Thank you in advance for taking this feedback into consideration and please do not hesitate to contact me should you have any questions or wish to receive any additional information. We look forward to seeing the final IACG report and recommendations that will be submitted to the UN Secretary-General in April 2019.

Best regards, Lara

Lara Pandya MSci, MPH

Strategic Partnerships Officer

European & Developing Countries Clinical Trials Partnership (EDCTP)

European Association of Hospital Pharmacists (EAHP)



Response of the European Association of Hospital Pharmacists to the public discussion on the draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance

The European Association of Hospital Pharmacists (EAHP) welcomes the World Health Organisation's (WHO) "Draft recommendations of the Ad hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance". This action-oriented initiative is extremely important in light of growing worldwide evidence on the considerable socio-economic threats posed by antimicrobial resistance (AMR) in the near future. In this sense, the IACG's mandate is vital in fostering and guiding efficient collaborative governmental action and providing highly needed global goals and targets on tackling AMR.

The EAHP is an umbrella organisation that represents more than 22,000 hospital pharmacists in 35 European countries which aims at ensuring continuous improvement of care and outcomes for patients in the hospital setting. From this point of view, the global response against AMR is a priority for the hospital pharmacy community and, in line with the EAHP's AMR position paper, it is able to provide specific suggestions for the hospital setting where acute care patients are among the most at risk.

As outlined in the European Statements of Hospital Pharmacy,² hospital pharmacists play a central role in optimising patient outcomes through working collaboratively in multidisciplinary teams – such as for instance stewardship teams. They are directly involved in the compounding and procurement of medicines in line with principles on safety, quality and efficacy.³ In addition, hospital pharmacists can provide expertise in developing, monitoring, reviewing and improving medicine use processes, related technologies and medicines formulary systems at local, regional and national levels.⁴

On the need to address shortages and stockouts (*Section A, Recommendation A1*, *bullet point 2*, *sub-bullet point 1 to 3*, *page 4*), the EAHP would like to point out that its 2018 Medicines Shortages Survey⁵ revealed significant shortcomings throughout Europe. 77% of participants indicated antimicrobial agents (specifically, the antimicrobial Piperacillin/tazobactam) as being most commonly in shortage in hospitals, followed by 43% reporting preventive medicines (such as vaccines). The responses for these two particular areas of medicine signal that access to both antimicrobials and vaccines must be prioritised when dealing with AMR. Tackling AMR is a global endeavour and the current national, as well as the envisaged European, notification systems should be interlinked with similar tools present in other countries around the world in order to ensure uniform dissemination and response. From this point of view, the IACG is best positioned to encourage all stakeholders to engage more practically in discussing and implementing clear and detailed action-oriented plans that would necessarily include a strong component on transparent, coherent and constant communication channel between all stakeholders.

¹ EAHP's position paper on antimicrobial resistance from June 2018 available at: http://www.eahp.eu/practice-and-policy/antimicrobial-resistance.

² EAHP's 44 European Statements of Hospital Pharmacy express commonly agreed objectives which every European health system should aim for in the delivery of hospital pharmacy services. The European Statements of Hospital Pharmacy are available at: http://statements.eahp.eu/statements/final-statements.

 $^{^{3}}$ This is in line with EAHP Statements Section 3 "Production and compounding", paragraphs 3.1 to 3.6.

⁴ This is in line with EAHP Statements Section 2 "Selection, procurement and distribution", paragraphs 2.1 to 2.5.

⁵ EAHP's 2018 Survey on Medicines Shortages to improve patient outcomes, available at: http://www.eahp.eu/practice-and-policy/medicines-shortages/2018-medicines-shortage-survey.



The EAHP would like to outline the following suggestions, based on key hospital needs in the response to AMR that should be considered by the IACG.

In general a clarification on the stakeholders covered by the IACG draft recommendation is needed for the preparation of responses at national and local level. Such information is in particular relevant for national action plans which detail the procedures and activities that the responsible actors need to undertake and with whom these actions need to be coordinated. EAHP would suggest to incorporate a reference to healthcare professionals in the "Guiding principles", bullet point 5 (page 3).

Vis-à-vis Section A, Recommendation A1, bullet point 1 (page 4), the EAHP would like to propose including a specific mention on the need for governments and regional entities to actively involve healthcare professionals, such as hospital pharmacists, who possess knowledge and practical expertise in medication procurement, formulary development and management, as well as pharmacoeconomic analysis and patient safety. Moreover, the notification systems mentioned in sub-bullet point 1 should be interlinked with similar tools present in other countries around the world in order to ensure uniform dissemination and response.

Regarding Section E, Recommendation E1 (page 14) referring to the establishment of a One Health "Leadership Group on Antimicrobial Resistance", the EAHP would like to recommend further clarification on the composition of the leadership group. Hospital pharmacy experts should be included among the stakeholders since they possess the necessary technical and practical knowledge to provide well-founded technical, but also policy response suggestions and precise interventions.

The EAHP would like to propose the inclusion of hospital pharmacists in the Independent Panel on Evidence for Action against Antimicrobial Resistance mentioned in Section E, Recommendation E2, bullet point 3 (page 16). As specialised healthcare professionals, hospital pharmacists can assist in matters pertaining to medication management and patient safety as well as in running clinical trials and drug research. Hospital pharmacy experts can translate the collected data into effective policy interventions (bullet point 1 of Section E, Recommendation E2, page 16), as well as contribute to periodic technical reports (bullet point 2 of Section E, Recommendation E2, page 16).

Regarding Section E, Recommendation E3 (page 16 and 17), which refers to the need to provide adequate and sustainable core funding for AMR activities, the EAHP would welcome the inclusion of a reference to healthcare professionals' initiatives on AMR, such as antimicrobial stewardship (ABS) teams in the hospital setting, in particular in bullet point 4 (on drawing lessons from experience and best practice models of the Tripartite agencies) and bullet point 5 (on conducting Joint Periodic Review missions on AMR within the One Health context). ABS should receive adequate and sustainable core funding and support to facilitate the dissemination of best practice initiatives, information exchanges, country visits for AMR experts who can offer guidance and capacity building activities. There are solid scientific results coming from both independent experts and international institutions on the efficient reduction of antibiotic overdose, positive contributions to resistance development and cost benefits achieved through the use of ABS teams.

Similar to Section A, Recommendation A1, bullet point 1 (page 4) also for Section E, Recommendation E4, bullet point 2 (page 18) the EAHP would like to propose the active engagement of healthcare professionals in the discussion on the "Global Development and Stewardship Framework to Combat Antimicrobial Resistance". In particular the knowledge and expertise of hospital pharmacists in medication procurement, formulary development and management, as well as pharmacoeconomic analysis and patient safety could enrich these discussions.



The EAHP would like to underline that hospital pharmacists already contribute to international efforts by participating in the development of antimicrobial stewardship toolkits commissioned by the European Centre for Disease Prevention and Control that are currently being used throughout the European Union. Hospital pharmacists are therefore willing and able to provide professional input and guidance to all responsible (inter)national entities and to work in multidisciplinary stewardship teams that monitor and tackle this problem at patient level.

The EAHP's precise recommendations can be summarised in the following manner:

- 1. Healthcare professionals should be specifically mentioned as a key stakeholder group that should be mobilised at all policy levels (global, regional, national, local), alongside governments, international organisations, academia, civil society and the private sector (section "Guiding principles", bullet point 5, page 3)
 Subsequent national and local-level action plans will need to detail the procedures and activities that
 - Subsequent national and local-level action plans will need to detail the procedures and activities that the responsible actors need to undertake and with whom they need to coordinate and collaborate at the local, regional, national and international levels;
- 2. **Develop the involvement of hospital pharmacists at hospital level** (Section A, Recommendation A1, bullet point 2, page 4)
 - Hospital pharmacists are among the key actors who must be involved throughout the surveillance and decision-making channels since they can contribute in addressing potential gaps and bottlenecks in responding to AMR;
- 3. **Develop digitally interoperable and safe communication channels** (Section A, Recommendation A1, bullet point 2, sub-bullet pint 1, page 4)
 - All national, European and global efforts in tackling shortages of antimicrobials and vaccines should be doubled by solid and digitally interlinked information channels, as well as consistent communication strategies in order to ensure uniform dissemination and response;
- 4. Involve hospital pharmacy experts in international-level expert groups (Section E, Recommendation E1, page 14; Section E, Recommendation E2, bullet point 3, page 16; Section E, Recommendation E4, bullet point 2, page 18)
 - Hospital pharmacists should be among the key stakeholders involved in the One Health "Leadership Group on Antimicrobial Resistance", the Independent Panel on Evidence for Action against Antimicrobial Resistance and the "Global Development and Stewardship Framework to Combat Antimicrobial Resistance" since they can contribute in closing potential gaps and bottlenecks in responding to AMR;
- 5. Place more emphasis on the need to increase the use of ABS teams in hospitals (Section E, Recommendation E3)
 - Engaging in ABS teams has a proven track record of lowering negative consequences of poor antibiotics use in patients while also decreasing overall costs. In addition, ABS team member also help mitigate antibiotic shortages in a way, which will optimise patient treatment and direct scarce financial resources.

Jean Carlet, President, World Alliance Against Antibiotic Resistance

From: <u>Jean Carlet</u>
To: <u>IACG-secretariat</u>

Cc: SPRENGER, Marc; Jacques Acar; SALOMON, Jérôme (DGS)

Subject: Re: Discussions with Civil Society Organizations on the draft IACG Recommendations

Date: Tuesday, February 12, 2019 18:41:45

Dear

Please, find herewith my proposals for the IACG document. I am president of a large international NGO, called the "World Alliance Against Antibiotic Resistance" (WAAAR), gathering 750 members from 57 different countries, and supported by 125 scientific societies or various groups involved in AMR. My name is Jean Carlet, MD,

Comments

- 1) The aim of antibiotic stewardship and of national campaigns is not only to reduce antibiotic consumption, but rather to provide to patients an appropriate antibiotic treatment, when needed. In many cases, no Ab are given although they would be needed. Very often, the wrong antibiotic is prescribed. This must be assessed on a regular basis in both the hospitals and the community. On the same line, it would be important to collect information on the failures of antibiotic therapy, and on the deaths of patients infected, but not receiving any antibiotics. It is a theoretical risk of the campaigns aimed at reducing antibiotic usage.
- 2) Most studies and recommendations concern the hospitals. It is imperative to look more carefully at the usage of antibiotics in the community (GPs), since 80 to 90% of the consumption is coming from this sector. In particular, the use of the available diagnostic tests is very low in most countries (Strepto test, CRP, PCT...)
- 3) The importance of the consumers and patients is mentioned in the IACG document, but this topic is key, and should be further developed. Their role is key in the construction and implementation of national or international actions and recommendations.
- 4) National campaigns must be organized on a regular basis, in order to improve the education on AMR, for both the public and health care professionals. The effect of a given campaign is not sustained enough.
- 5) The use of ALL antibiotics must be forbidden for growth promotion in ALL countries, without any delay, and not for certain antibiotics, as proposed in the report
- 6) It is of paramount importance to set up, in all countries, inter-ministerial structures on the issue of AMR, since many ministries are concerned by this threat. Some excellent recommendations are often proposed by the ministries of health, but are never implemented, since they are blocked by other ministries, in particular the ministries of finances. A global, and consensual program is mandatory, in a "one health" philosophy.
- 7) Research efforts are urgently needed, but they must be also concern the access to new rapid diagnostic tests, and alternatives to antibiotics. The tests allowing to distinguished viral from bacterial infections, in particular for respiratory infections

I do hope that the IACG will find those comments useful, and I am ready to further help in any way. *I want to* attend the different events scheduled, including the meetings in Geneva and in New York

Very best regards Dr Jean CARLET

Keep Antibiotics Working (KAW)



The Campaign to End Antibiotic Overuse

www.KeepAntibioticsWorking.org

KEEP ANTIBIOTICS WORKING COALITION (KAW) RESPONSE TO THE PUBLIC CONSULTATION ON THE DRAFT RECOMMENDATIONS OF THE INTERAGENCY COORDINATION GROUP ON AMR (IACG)

February 19, 2019

Submitted by Steven Roach, Food Safety Program Director, Food Animal Concerns Trust, Keep Antibiotics **Working Coalition Member**

Keep Antibiotics Working (KAW) appreciates the opportunity to comment on the Draft Recommendations of the Interagency Coordination Group on AMR. Formed in 2001, KAW is a coalition of seventeen advocacy groups that work together to ensure that untreatable superbugs resulting from the overuse of antibiotics on farms do not reverse the medical advances of the past century. Since the focus of our work is on resistance that results from the use of antibiotics in agriculture, KAW's comments will focus on this area.

KAW is disappointed that the IACG recommendations do not more clearly match the recommendations of the 2017 World Health Organization (WHO) guidelines on use of medically important antimicrobials in foodproducing animals. Instead, the recommendations for action on agriculture more closely match the much older recommendations from the 2000 WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food². The IACG draft recommendations read as if the international community has not learned anything in the last nineteen years despite the increasing seriousness of the problem. Since 2000, we have detected the global spread in food and farm animals of extended-spectrum beta-lactamase producing Enterobacteriaceae, methicillin resistant Staphylococcus aureus, and colistinresistant Enterobacteriaceae among many others. While the problem has gotten worse, the recommendations have not been strengthened.

KAW calls upon the IACG to include recommendations consistent with the 2017 WHO guidelines. We ask that the IACG recommendations direct Member States to 1) set targets for reductions in overall antibiotic use in agriculture, 2) immediately phase out the use of medically important antibiotics for growth promotion and routine disease prevention, and 3) restrict the use of highest priority critically important antibiotics to individual animal treatment or in the case of the last resort drug colistin ban its use altogether.

KAW also asks the IACG consider how the recommendation that risk analysis be used in making decisions related to antimicrobial use in animal agriculture has hindered action aimed at protecting public health and is inherently biased against low-income countries. Risk analysis particularly with respect to antibiotic resistance is a very resource intense activity and thus is conservative in nature. Globally, when countries have made

¹ https://www.who.int/foodsafety/areas work/antimicrobial-resistance/cia guidelines/en/

² https://www.who.int/foodsafety/publications/containment-amr/en/

decisions to restrict antibiotic use in food producing animals to protect public health they often have not used formal risk assessment and risk analysis. When they have used risk analysis, it has often been challenged by drug makers and led to long drawn out legal challenges (e.g. fluoroquinolone withdrawals by U.S. Food and Drug Administration). Risk assessment related to antimicrobial use has primarily been carried out by high-income countries as part of the registration process for new drugs or new uses of previously approved drugs.

Because risk analysis is so resource intensive, the recommendation for risk analysis creates a bias against low and middle-income countries when addressing antibiotic use. This was illustrated at the sixth Meeting of the Codex Alimentarius Task Force on Antimicrobial Resistance where low income countries protested as unfair inclusion in a guidance document of national or regional lists of medically important antibiotics. High-income countries have carried out risk assessments and used these to move certain animal drugs (e.g. bacitracin) from their national list of medically important drugs and thus continue to use them for growth promotion while low-income countries rely on the WHO list of critically important antimicrobials. Similarly, low-income countries rely on Codex Alimentarius for setting residue limits, but Codex Alimentarius has so far not conducted any risk analysis itself that could be used to guide countries in making decisions related to antimicrobial resistance with respect to veterinary drugs. This leads to a situation where the use of a drug in the production of food is considered safe under international standards because it does not lead to a residue risk even though the use may not have been evaluated for the much greater risk related to antimicrobial resistance.

Need for national reduction targets for antibiotics used in agriculture

Goals are essential for addressing public health challenges and given the high risk to public health and the abundant evidence that the overuse of antibiotics is common in agriculture settings national targets for reductions in antibiotic use in agriculture should be part of the IACG recommendations. These targets should be based on measures that take into account both the animal population and the amounts of antibiotics used or sold. Targets should be specific to different livestock sectors and there should be separate targets for high priority drugs to protect the efficacy of these drugs for animal and human health. Setting national reduction targets is consistent with Recommendation 1 of the 2017 WHO Guidelines.

Need for a clear recommendation to eliminate the use of antibiotics for growth promotion without caveats for risk analysis

The phasing out of the use of medically important antibiotics for growth promotion was a recommendation of the 2000 WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food. Almost 20 years later this recommendation should not be controversial. KAW believes that the language in the Global Principles allowing for continued use of growth promoters after a risk assessment has contributed to the long delay in phasing out these uses. This likely has led to the current situation with very high levels of resistance in farming systems where antibiotics have been used routinely for growth promotion. Eliminating the use of antibiotics for growth promotion is consistent with Recommendation 2 of the 2017 WHO Guidelines.

Need for a clear recommendation to eliminate the use of medically important antibiotics for disease prevention

Eliminating antibiotics for use as growth promoters is important but is clearly not enough. There are numerous examples globally about very problematic uses of medically important antibiotic antibiotics for disease prevention that will not be addressed by eliminating their use for growth promotion and calling on individual countries to carry out risk analysis. In the United States, over 70 percent of cattle on large feedlots receive the highest priority critically important antimicrobial tylosin in feed on average for 170 days as a routine

preventative for liver abscesses³. In Belgium in 2010, researchers found that over 90 percent of feed medications were for disease prevention not treatment and that this use was often of critically important drug⁴. A 2016 news article describes how farmers in India use a mixture of the highest priority critically important drugs enrofloxacin, ciprofloxacin and colistin to prevent respiratory disease⁵. A survey in Thailand found farms routinely using a mixture of five drugs including the highest priority critically important drugs colistin and tilmicosin for disease prevention. A growth promoter phase out will doing nothing to address these uses. Eliminating preventive use is consistent with Recommendation 3 of the 2017 WHO Guidelines.

Need for clear recommendation to restrict the use of the highest priority critically important antimicrobials (HPCIAs) Highest priority critically important antibiotics are ranked this way because there is a need to improve how they are used in food animals. When resistance develops to these drugs, there is a very high risk that it can seriously harm human health. One of these drugs, colistin, is a drug of last resort that is used in humans when nothing else works. There is also very clear evidence that the use of colistin and related drugs in animals is linked to the spread of transferable resistance to this drug globally⁶. Consistent with the 2017 WHO Recommendation 4, KAW asks for a recommendation from the IACG that HPCIAs only be used for individual animal treatment after susceptibility testing indicates they are needed and that colistin and related drugs not be used in agriculture at all.

Suggested language

KAW recommends the following rewording of Recommendation A3:

IACG calls on Member States to reduce use of antimicrobials in food animal and plant production with targeted reduction goals determined by countries' specific conditions. Member States should end use of medically-important antimicrobials for growth promotion purposes consistent with WHO's Guidelines on Use of Medically-Important Antimicrobials (MIAs) in Food Producing Animals. In addition, Member states should end use of MIAs for disease prevention purposes except where a veterinary professional judges there is a high risk of spread of a specific infectious disease, based on a recent culture and sensitivity testing results. Antimicrobials should only be used to treat or control disease, consistent with the guidance of tripartite agencies (FAO, OIE and WHO). Finally, use of Highest Priority Critically Important Antimicrobials (i.e., quinolones, third and higher- generation cephalosporins, macrolides and ketolides, and glycopeptides) should immediately end for growth promotion, disease prevention and disease control in food animal or plant production and should be permitted for individual animal disease treatment only if it is the only treatment option as determined by recent culture and sensitivity testing results. The last resort drug colistin and other polymyxins should not be used in agriculture."

3

³ https://www.aphis.usda.gov/animal health/nahms/feedlot/downloads/feedlot2011/Feed11 dr PartIV.pdf

⁴http://www.abcheck.ugent.be/v2/download/Prophylactic%20and%20metaphylactic%20antimicrobial%20use%20in%20Belgian%20f attening%20pig%20herds%20-%20B%20Callens.pdf

⁵ https://www.bloomberg.com/news/features/2016-03-29/antibiotic-apocalypse-fear-stoked-by-india-s-drugged-chickens

⁶ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5862964/

Korean Society for Antimicrobial Therapy

Proposal for Antibiotics Regulation System

Antibiotics resistance affects not one but many areas that include humans, animals, and the environment. Moreover, an antibiotic administered on one individual and the resistance thereby developed has an effect on other individuals as well. In this line of cause and effect, antibiotics can be considered a medicine of the public sphere, and therefore to be regarded as a public medicinal product with its use to be controlled as a matter of public safety.

- 1) The critical center of antibiotics resistance suppression and antibiotics stewardship is decreasing the use of antibiotics: Antibiotic-resistant bacteria spreads to all humans, animals, and environment, but what increases the rate of antibiotics resistance is ultimately when overuse of antibiotics generates selectivity with regard to antibiotics-resistant bacteria.
- 2) The efforts to decrease the use of antibiotics must be first and foremost among humans: Suppression of antibiotics use must be applied in all areas to be certain, and includes humans, animals, as well as the environment. However, the most urgent need for suppression is among humans.
- **3)** Antibiotics stewardship at the level of hospitals is important in suppressing multiple-drug resistance: Antibiotics policies at primary care medical institutions would be essential in light of the fact that gross amount of antibiotics usage is larger in those primary care institutions. But typically, multiple-drug resistant organisms such as ESBL(+)GNB, CRAB, CRE, MRSA, VRE are prevalent mainly in the secondary and tertiary medical institutions. Henceforth, antibiotics stewardship at hospital-level medical institutions should play a major role in suppressing the increase of multiple-drug resistant bacteria.
- 4) All antibiotics must be the subject of antibiotics stewardship applied at hospital-level medical institutions.(All antibiotics must be regulated as restricted antibiotics.): CRE is associated with the overuse of Carbapenem, overuse of Carbapenem is due to increase of ESBL(+)GNB, and the increase of ESBL(+)GNB is associated with overuse of Cephalosporin. In other words, unless all antibiotics are regulated at hospitals as restricted antibiotics, it becomes difficult to suppress the increase of any multiple-drug resistant bacteria.
- 5) Execution of the legislative antibiotics regulation policies is necessary: If stewardship is to be practically applied and operated at hospitals on all antibiotics, antibiotics-specialist pharmacists and antibiotics-regulator nurses need to be nurtured and made available. If there is a lack of specialists from this field, then one may consider the alternative of training non-related medical professionals for a set period of time and assigning them to the operations of antibiotics regulation.

(Example) Organization of Antibiotics Stewardship System at Hospital-level Medical Institutions

1) Members

- 1 or more infectious diseases specialist physician, 1 or more antibiotics-regulator pharmacist, antibiotics-regulator physician(s) (less than 300:1 ratio by number of beds), antibiotics-regulator nurse(s) (less than 150:1 ratio by number of beds)

2) Qualifications for Membership

- Infectious diseases specialist physician: Board-certified physician of infectious diseases, board-certified physician of pediatrics in the infections division
- Antibiotics-regulator physician: Board-certified physician of infectious diseases, board-certified pediatrics physician of the infections division, or physician who received education of 12 hours or more on antibiotics regulation and must receive Continuing Medical Education (CME) of 8 hours annually
- Antibiotics-regulator pharmacist: Antibiotics specialist pharmacist, or pharmacist who received education of 12 hours or more on antibiotics regulation and must receive Continuing Medical Education (CME) of 8 hours annually
- Antibiotics-regulator nurse: Antibiotics-regulator nurse, or nurse who received education of 12 hours or more on antibiotics regulation and must receive Continuing Medical Education (CME) of 8 hours annually

3) Responsibilities

- Infectious diseases specialist physician: Must be the overall supervisor of all antibiotics regulation, must lead in the holding of more than one monthly antibiotics regulation committee meetings, must decide the hospital's antibiotics policies.
- Antibiotics-regulator physician: Must receive reports on patients using antibiotics from the antibiotics-regulator nurse, must administer appropriate antibiotics usage through the family doctor.
- Antibiotics-regulator pharmacist: Must report more than once monthly on the actual state of antibiotics use, must co-function with the infectious diseases specialist physician on all of antibiotics regulation.
- Antibiotics-regulator nurse: Must daily evaluate patients who are using antibiotics, must report to the antibiotics-regulator physician upon cases of inappropriate antibiotics usage as determined as such by the antibiotics usage guideline.

MSF Access Campaign

MSF Access Campaign FEBRUARY 2019



MSF Access Campaign response to the public discussion on the draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance (IACG)

Overview

Médecins Sans Frontières (MSF) welcomes the opportunity to provide comments on the draft recommendations of the IACG ahead of the report's submission to the UN Secretary-General by April 2019.

As a medical humanitarian organisation with operations in over 70 countries, MSF is deeply concerned by the rapidly growing global burden of antimicrobial resistance (AMR) – a highly complex health challenge that defies borders and spares no one. Among those disproportionately affected are the poor, rural, neglected, conflict- and disaster-affected populations that are our primary concern. Our efforts to draw attention to the problem of AMR in the settings where we work have helped us understand that drug-resistant infections are present and spreading everywhere. We see this evidence directly when we identify resistant bacteria in the blood of newborn babies in West Africa or the bones of war-wounded patients in the Middle East – and we see it indirectly when our best available anti-infective treatments fail or we witness the widespread misuse of antimicrobials, particularly through their unregulated sale.

From Iraq to India, Yemen to Sudan, and from Syria to the Central African Republic, wherever we have looked for evidence of AMR, we have found it. We therefore acknowledge with respect and appreciation the efforts of the IACG to date, but feel compelled to point out some key areas within this critically important work where the needs of our patients and healthcare professionals remain inadequately addressed.

Overall, it is encouraging to see that this draft is anchored in the 2016 UN Political Declaration on Antimicrobial Resistance, and that many of the principles set out in the Declaration are taken into account. This is evidenced in the considerations for recommendation B1, where the IACG reiterates that "...all research and development efforts to address antimicrobial resistance should be needs-driven, evidence-based and guided by the principles of affordability, effectiveness, efficiency and equity". However, we note with concern that this current draft does not reflect the UN Political Declaration's prioritisation of "... the importance of delinking the cost of investment in research and development on antimicrobial resistance from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools, vaccines and other results to be gained through research and development..." High medicines prices due to unchecked monopoly powers and the consequent access challenges have become a globally recognised issue – from pneumococcal vaccines to newer drugs for the treatment of hepatitis C virus and cancer. Given the massive injection of public and philanthropic funding into R&D for drugs, diagnostics and vaccines to address AMR, it is critical to establish novel approaches on pricing based on the full transparency of underlying costs and recognising the collective effort of different contributors to the R&D process, from basic research to implementation and patient access.

Moreover, as discussed below in relation to the recommendations outlined under Section B, "Innovate to Secure the Future", we urge the IACG not merely to reference the principles of the UN Political Declaration, but to provide concrete guidance as to how such principles can be adhered to. Given the unfortunate disconnect between the noting of the Declaration's principles and the considerations on incentives that are subsequently elaborated, the draft recommendations do not adequately reflect the guiding principles of the Declaration.

The manner in which this report's recommendations and considerations will be taken forward remains an unanswered question. Much of the guidance to governments is listed as a "consideration for this recommendation", but is written in the form of a recommendation that "governments should establish...". Further clarity is needed to ensure that some of the important "considerations" are not treated merely as footnotes, but are taken up as recommendations.

Below we provide comments on several of the specific recommendations and considerations outlined in the report.

Section A: Accelerate progress in countries

Recommendation A1: "The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health."

- The headline objective focuses exclusively on antimicrobials, whereas under "considerations for the recommendations" this is expanded to cover drugs, diagnostics and vaccines. We support the wider focus, as it is right to focus on all three technologies. Increasing affordable access to vaccines should be a high priority within the global AMR response as there is overwhelming evidence supporting vaccination as an effective, safe, low-cost measure to reduce the burden of both infectious diseases and AMR at every level. For example, it has been estimated that introduction of the Haemophilus influenzae type b (Hib) conjugate vaccine and pneumococcal conjugate vaccine (PCV) to 75 developing countries could reduce antibiotic use for these diseases by 47% and avert 11.4 million days of antibiotic use each year in children younger than 5 years of age. MSF has been campaigning for several years for more affordable versions of PCV to be made available to developing countries and humanitarian organisations. This is something the IACG should concretely support.
- We strongly support the recommendation on "Establishing antimicrobial production facilities", that "governments or regional entities may consider establishing production facilities or contracting manufacturers to help mitigate shortages and ensure a resilient supply of antimicrobials, particularly antibiotics and vaccines for human and animal health, paying due consideration to manufacturing standards and quality assurance for health commodities." It is clear that market forces are not serving the interests of patients and healthcare professionals in the case of AMR. In many countries where we work, MSF sees that certain essential ACCESS antibiotics are not adequately available, while other WATCH and RESERVE antibiotics are freely available without sufficient controls. Market exits, inflexible production cycles, and sole-sourcing negatively affect access to basic antibiotics internationally. Several manufacturing sites, including those of international pharmaceutical companies, are ceasing production of basic essential antibiotics deemed 'not viable'. Meanwhile, global demand for drugs such as penicillins is not adequately secured. The above recommendation calling on governments and regional entities to consider solutions beyond the market, such as establishing production facilities or contracting manufacturers to ensure a resilient supply of antimicrobials, is a welcome practical solution.
- The challenges identified in this section for global shortages of existing antibiotics will also be faced for new antibiotics in development that are indicated for WATCH and RESERVE use. We know from the situation described above that relying on market forces will not deliver what is needed by patients and healthcare professionals when it comes to treating infections appropriately. This must be acknowledged, and whether in terms of contract manufacturing, direct establishment of production facilities or other initiatives, we must start designing measures to prevent shortages and stockouts, ensure a sustainable supply of critically needed antimicrobials and vaccines, and facilitate the rationale manufacture and supply of antibiotics that have not yet been developed or attained marketing authorisation. These measures must start with those public health goals in mind and, as such, look for solutions beyond the market.
- We support the recommendation on "Pooled procurement mechanisms: Leveraging existing pooled procurement mechanisms in human health and potentially establishing them for animal health could help to secure both the supply of quality-assured medicines and ensure predictability of demand for manufacturers." Pooled procurement mechanisms such as the Global Drug Facility (GDF) model should be explored as a mechanism for ensuring both lower prices for antibiotics and improved stewardship in the immediate term. GDF represents a large portion of the market for TB drugs and diagnostics, and uses this to negotiate prices with companies based on larger volumes. GDF's international tenders allow both generic and originator companies to compete in supplying quality-assured TB medicines. GDF rejects tiered pricing, encourages suppliers to enter into markets, provides forecasting to suppliers, and provides governments with forecasting assistance and orders (which is important given different shelf lives). It anticipates and addresses global supply issues and provides advice to countries on switching from suboptimal to optimal formulations. In the area of diagnostic tools, GDF has been able to negotiate improved service and maintenance terms from companies.
- We highlight with concern the final consideration outlined with regard to ensuring equitable and affordable access to and stewardship of existing and new quality-assured drugs, diagnostics and vaccines: the assertion that, "complementary efforts to improve antimicrobial resistance surveillance and supply chain mechanisms including the implementation of low-cost technologies and track-and-trace systems could

help to address [the problem of substandard and falsified medical products] in low- and middle-income countries." Tackling this complex problem requires extensive work on regulatory systems strengthening. There are no silver bullets when it comes to building strong, resilient regulatory systems. Implementing track-and-trace systems in the absence of such regulatory work is doomed to failure.

Section B: Innovate to secure the future

Recommendation B1: "The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials - particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials - for human, terrestrial and aquatic animal and plant health..."

- MSF welcomes the call for an increased investment in innovation in new antimicrobials, antibiotics, diagnostics and vaccines, as well as waste management tools and safe and effective alternatives. However, as stated in our response to the previous IACG consultation, investments in R&D should not focus exclusively on bringing new antibiotics, diagnostics and vaccines to market, but also on other areas of innovation that are needed to effectively combat AMR. This includes (1) the repurposing of older or withdrawn antibiotics, (2) exploring the as-yet-untapped potential of both combination products (rational FDCs) and non-traditional therapeutics (such as antibody and phage therapies), (3) sustainably implementing new technologies within health programmes, and (4) developing novel approaches and clinical algorithms that are adapted to the local context. It also requires adapting existing drugs to the needs of specific patient populations that are often overlooked, such as the development of heat-stable, paediatric and oral formulations of existing and new antibiotics. For example, there is a lack of narrow-spectrum oral drugs to treat defined diseases that are commonly caused by antibiotic resistant bacteria, such as UTIs or typhoid. The IACG must recognise the need for financial support for the above areas of work and not focus too narrowly on 'new tools'.
- We would further suggest including a recommendation to the WHO to establish global priorities in the above areas of unmet medical need, in order that R&D funding can be aligned accordingly.
- While we welcome the statement under recommendation B1 that incentives be "...based on the principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance", we note with concern that no guidance is provided as to how these principles can be met. We believe that the IACG should provide such guidance.
 - o For the principle of affordability, for example, the IACG should advocate for the attachment of conditions for access to public and philanthropic R&D funding. Funding for upstream R&D can and should be coupled with access and stewardship requirements downstream as these products enter the market. Medicines that have benefited from significant public support should be considered public goods, and this collective investment should be secured through affordability and accessibility for all. To enable affordability, the IACG should recommend that public funders ensure the traceability of taxpayer money invested in R&D. This is a necessary prerequisite for providing transparency and building public accountability for R&D as a shared responsibility.
 - o The principle of efficiency can be ensured by fostering collaboration in order to accelerate delivery time of new treatments from 'bench to bedside' through (1) sharing research results, including clinical trial data, (2) providing access to well-characterised sample banks and compound libraries, and (3) pooling intellectual property rights as needed to further optimise development. These conditions will expedite development, reduce costs, and increase efficiency. DNDi have piloted many of these approaches to collaboration, so can be looked to to provide concrete examples of best practice in this area. The IACG should recommend incentives that foster these approaches.
 - The principle of equity can be addressed by ensuring that funding is made available for adapting drugs to the needs of specific patient populations that are often overlooked such as children and pregnant women as we have outlined above.
- The first consideration outlined under this recommendation focuses too narrowly on 'market pull' incentives as a means to address the lack of innovation in the area of antibiotic, diagnostic and vaccine development. Such pull incentives are often narrowly focused on the attainment of market authorisation. Given the current meagre state of the antibiotic pipeline, with only very few innovative compounds in all stages of development, MSF would argue that this focus is misplaced. We emphasise that it is important to

ensure that the prioritisation of funding allocations is targeted towards overcoming scientific barriers and bottlenecks and ensuring demonstrable therapeutic advance. As such, it is worth considering increasing the amount of funding available in grants to those involved in upstream, early-stage drug discovery and development.

- The process of prioritisation in antibiotic R&D has to be needs-driven, use the WHO Priority Pathogen List as a starting point, and assess the therapeutic benefit of potential leads for patients based on the definition of innovativeness provided in the WHO analysis of the antibacterial clinical development pipeline, including *Mycobacterium tuberculosis*. This is critical, as a majority of the agents currently in the pipeline are 'me-too' modifications of molecules that are currently marketed; a majority of others are modified agents of known antibiotic classes. If widely used, modified agents of old drug classes can drive rapid development of cross-resistance and co-selecting resistance.
- The "considerations" further note that, "the IACG recognizes the need to develop and provide financial and non-financial market incentives for research and development to address antimicrobial resistance...". As stated above, there is a need to look beyond the market when it comes to finding the appropriate means of stimulating the necessary R&D to address AMR. A focus on market-fixing can lead to expensive solutions that hone in narrowly on one particular challenge in the product life cycle, while failing to address equally important aspects further along. For example, a focus on pull incentives that aim to fast track the registration of novel antibiotics can be very costly (especially if the pull attempts to provide an incentive that competes with otherwise commercially attractive areas of investment¹, such as oncology), but since the incentive is only focused on the achievement of registration in one or two markets, it neglects a very large part of the development challenge that is to ensure that products are not only registered in all countries in need, but are manufactured in sufficient quantities and not commercially marketed (but instead are appropriately stewarded). Few late-stage antibiotics currently have any form of access or stewardship plans: three have access plans; two have stewardship plans; two have both access and stewardship plans. This of course says nothing about the quality of such plans, which must also be examined.

Recommendation B2: "The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health."

- MSF is concerned that this recommendation focuses on "leveraging existing global access and scale-up initiatives in human health", without proposing how the significant gaps that currently exist in these initiatives will be filled. That is to say, the report identifies CEPI, Gavi, Global Fund to Fight AIDS, Tuberculosis and Malaria, Medicines Patent Pool, and Unitaid as the examples, yet does not highlight that these initiatives currently lack a specific focus on AMR. While some of these initiatives cover certain aspects of the AMR challenge such as HIV, TB and malaria they do not as yet cover the full scope of AMR.
- Moreover, the scope of countries covered by these initiatives is limited and differs from one to the other. In recent years, these funds have insisted on 'transitioning' or 'graduating' middle-income countries out of eligibility for support. As such, the usefulness of these funds to address the access issues of a wider range of countries is further diminished. The IACG should recommend that any mechanism to expand access to AMR-related health technologies be global in scope. This could start with revisiting and reversing the current trend towards restricting support for LMICs through 'graduation' and 'transition'.
- Without significant additional investment, it is difficult to see how these organisations will be able to meet their existing mandates let alone expand to cover the full breadth of the AMR response.

Recommendation B3: "The IACG calls upon the public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context..."

• MSF supports the call within this recommendation for research funders to undertake a number of activities, such as a coordinated global mapping of research and development activities and funding to address AMR,

¹ In the Final Report and Recommendations of the Review on Antimicrobial Resistance, chaired by Jim O'Neill and published in May 2016, it is noted on page 6 that the global market for patented antibiotics is currently about \$US4.7 billion in sales per year. This compares unfavourably with the global oncology market, where just one top-selling cancer drug will command that level of sales. https://amr-review.org/sites/default/files/160525 Final%20paper with%20cover.pdf

and promoting openness and transparency in data from all research and monitoring and surveillance sources. We agree with the considerations outlined under this recommendation, which highlight (1) the lack of information, collaboration and transparency across different research and development activities, funding agencies and partners, and (2) the significant barriers this lack of transparency poses to advancing research and development.

• Clear actions should be proposed to address the lack of transparency in such initiatives, particularly those led by the public and philanthropic sectors.

Section C: Collaborate for more effective action

Recommendation C2: "The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector... in order to ensure [among other things] affordable access, prudent use and stewardship of antimicrobials; ethical production, distribution and marketing practices..."

- The recommendation notes, under considerations, that "...the urgency and threat posed by antimicrobial resistance demand significantly more action by and enhanced engagement of the private sector...".
- Yet both the recommendation and considerations stop short of recommending that governments adopt legally binding measures to regulate these actors, which must at a minimum be considered. Operational research conducted by MSF in resource-limited settings such as Afghanistan, Central African Republic, Democratic Republic of the Congo and Sudan has demonstrated that both prescribers and patients are often poorly informed about the role and risks of antibiotics. Furthermore, soon-to-be published MSF studies from West Bengal, India show that pharmaceutical company representatives are key providers of information to prescribers and that this information is typically biased and often misleading. This raises serious concerns about conflicts of interest, compromised patient care and unethical commercial practice. Legislation is needed not only to guide the introduction, labelling, pricing and distribution of antibiotics, but also their manufacture and promotion. Leaving this to voluntary measures is not working: over a year after the launch of the Industry AMR Alliance, only 4 of the 100 companies who have joined have stopped rewarding sales agents with bonuses based on the volume of sales of antibiotics.

Section E: Strengthen global accountability and governance

Recommendation E1: "The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance (GLG), supported by a Secretariat..."

The recommendation notes, under considerations, the proposed composition of the GLG as "...a small group of current and former Heads of State, Ministers of Agriculture, Health and Environment, Heads of the Tripartite agencies, other UN and international agencies, Heads of Regional Banks and other prominent global leaders and eminent persons representing human, animal and plant health, as well as food production and the environment."

- MSF notes that this proposal does not indicate whether private sector directors would be permitted under the umbrella of "other prominent global leaders and eminent persons". MSF urges the IACG to clarify that the inclusion of private sector directors in future global governance arrangements would be unacceptable due to conflicts of interest.
- If the decision is taken to establish a GLG, it will be essential to ensure the group's mandate is firmly anchored in the 2016 Political Declaration of the High-level Meeting on Antimicrobial Resistance (Resolution A/RES/71/3). There is a risk of mission drift if the GLG is not given this mandate for action.
- For MSF, it is essential that the needs of developing countries, and particularly neglected people, are not left behind in future global governance. This must be assured through a transparent, accountable governance structure led by and inclusive of all Member States that provides for civil society engagement, oversight and consultation.
- MSF agrees that processes for engaging all relevant actors must be created, but believes it is essential to draw red lines between the roles and responsibilities of different actors. We have addressed this above, under Section C.

Recommendation E2: "The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation."

- If such an Independent Panel is established, it will be essential to play close attention to potential conflicts of interest, and to have a clear and robust policy for dealing with any such conflicts should they arise.
- For the Panel to achieve its stated goal, it will need to be a trusted source of data and evidence, free of vested interests. It is also important the that the evidence generated by the Panel is comprehensive so that it can reliably inform prioritisation of interventions, including those targeting resource-limited settings.

Recommendation E4: "The IACG recognizes the ongoing process led by Member States to develop the Global Development and Stewardship Framework to Combat Antimicrobial Resistance and urges the Tripartite agencies... and UNEP to expedite its development in line with the scope described in the 2015 World Health Assembly resolution on antimicrobial resistance (WHA68.7)..."

- To ensure accountability and emphasise the need for policy coherence, there should be a clearer call for the IACG recommendations to be considered in the Global Development and Stewardship Framework (GDSF). The GDSF is needed to guide countries in the design of access and stewardship measures that are practical and meaningful at a country level. As such, it is critical that the GDSF fully takes into account and is designed to meet the access and stewardship needs of low- and middle-income countries.
- We support the final consideration put forward by the IACG that, "...ongoing discussions and finalization of the process to develop the [GDSF] can be used as an initial platform by Member States to advance a stepwise approach towards potential new, binding or non-binding international instruments. Such instruments may need to include a stronger focus on supporting the distribution and appropriate use of existing and new antimicrobial medicines, diagnostics, vaccines and other interventions, while also preserving existing antimicrobial agents, including using the WHO ACCESS, WATCH and RESERVE categorization of antibiotics." Lasting and binding commitments at the level of Heads of State are necessary to effectively respond to the challenge of AMR, and it is essential that the eventual legal framework to emerge from the GDSF negotiations overcomes the real challenge of potential non-adherence.

Natural Resources Defense Council (NRDC)

February 19, 2019

To: IACG Secretariat

iacg-secretariat@who.int

From: David Wallinga, MD, MPA

Senior Health Officer

Natural Resources Defense Council (NRDC)

Subject: Public Feedback on the IACG's Draft Recommendations

I am submitting these comments on behalf of the Natural Resources Defense Council (NRDC), a U.S.-based NGO with more than 700 scientists, attorneys, advocates, and other staff, plus over 3 million members and online activists. Among other things, we advocate for new policy and market changes to help mitigate and adapt to the global health crisis posed by antimicrobial resistance. We welcome this opportunity to provide feedback to the United Nations' Interagency Coordination Group on Antimicrobial Resistance (IACG) draft recommendations, as well as on key messages that we believe ought to be shared with the Member States along with those recommendations.

We urge the Secretary General, as well as the IACG, to communicate to the policymakers reading these final recommendations the urgency of the worsening global epidemic of antimicrobial resistance, and the immediate need for a strong, effective response to the medical, public health and national security crises created by it. It cannot be overstated that today's resistance crisis threatens not only enormous loss of life and economic losses, but also the practice of modern medicine as we know it. A stronger case can and must be made that this crisis therefore requires investment of a level of resources commensurate with the enormity of the challenge it poses.

Further, the Secretary General and the IACG should more clearly state that the proper stewardship of medically important antibiotics demands that all routine uses of these precious medicines be curbed. While in many places truly sick people still lack access to effective antibiotics, it also is apparent that perhaps 75 percent of the global sales of these same drugs are intended for non-treatment, growth promotion or disease prevention uses in groups of livestock or poultry (i.e., in the absence of any diagnosed disease).

Finally, the presentation of these recommendations to policymakers should strongly urge that explicit numeric country-level targets be set for reducing antibiotic overuse in both human and animal settings. Where aggressive targets have been set for reducing the routine, unnecessary use of antibiotics in livestock production — in the Netherlands, for example — overall reductions of 60 percent or more have occurred. Milestones for reaching these targets also are essential to ensure accountability.

The 'environmental' dimensions of the resistance epidemic are critical, and deserve elevation both within the recommendations, and as part of their presentation to policymakers. The success of any effort to curb antibiotic resistance, for example, will be hampered wherever the manufacture of antibiotics, their use, the disposal of unused antibiotics, and the treatment and management of manure containing antibiotics are allowed to be conducted in ways that create large environmental reservoirs of drug residues and resistance genes. By providing additional selection pressure, these reservoirs feed the more-rapid development and spread of drug-resistant bacteria to the human population.

Finally, your communications to policymakers should emphasize that successful efforts to address antimicrobial resistance likely will be ones that have taken a more holistic, or systems, approach that accounts

Curbing antimicrobial use in animal production

We strongly agree with the IACG that "the overuse and misuse of antimicrobials to **promote growth** and **routinely prevent disease** in healthy animals and crops without appropriate indication and the absence of good agricultural practices are contributing to the development and spread of antimicrobial resistance in both animals and humans".

In particular, we commend the IACG on its efforts (under <u>Recommendation A3</u>) to phase out antimicrobial use for growth promotion. The point of ending a purely economic use of medically important antibiotics is to better preserve their future effectiveness for treating the sick. As the WHO's guidelines on the use of antimicrobials in food animal production so clearly state: "We recommend complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion." The IAGC recommendations should state the goal just as clearly. Instead, while they call for phasing out of antibiotic use for growth promotion *consistent with Tripartite guidance*, the various forms of the latter guidance are often inconsistent and could therefore create unnecessary confusion and even loopholes.

Using the science-based logic behind <u>Recommendation A3</u>, (and the WHO Guidelines), the IACG should **extend the phase-out of growth promotion so as to include to all medically important antibiotics**, and not just the much smaller subset of critically important antibiotics that have been deemed of 'highest priority" (HPCIAs). McDonald's, one of the largest beef purchasers in the world, announced a new policy in December 2018 pertaining to beef purchasing in its top ten markets. That policy directly states: "Use of antibiotics defined by WHO as medically important antibiotics for human medicine are not permitted for the purpose of growth promotion in food-producing animals in the McDonald's Supply Chain."²

¹ See https://apps.who.int/iris/bitstream/handle/10665/258970/9789241550130-eng.pdf?sequence=1

² See https://corporate.mcdonalds.com/content/dam/gwscorp/scale-for-good/McDonalds Beef Antibiotics Policy.pdf.

We also urge that the IACG final recommendations **include a phase out of routine use of medically important antibiotics to prevent disease in groups** of food producing animals, and that policymakers be reminded of the importance of setting national targets and milestones for reaching this specific goal. While the IACG's draft recommendations already acknowledge that antimicrobials routinely used to prevent disease in healthy animals are contributing to the global spread of resistance, they fail to recommend any specific action to address that problem. Yet in October 2018, the European Parliament passed legislation which starting in 2022, will disallow the routine use of medically important antibiotics for disease prevention in groups of food-producing animals.³ This creates global precedent for addressing the antibiotic overuse problem comprehensively, rather than in a piecemeal fashion.

Like growth promoting antibiotics, it remains legal and commonplace in most Member States to feed antibiotics of medical importance routinely to groups of food producing animals to prevent disease, even where no specific disease has been diagnosed. Many of these antibiotics are identical or very similar to growth promotion products, and are being fed to groups of animals within the same dosage range as growth promoters, often without any limits on their duration of use. In not directly speaking to these practices, the IACG's recommendations open the door for producers who want to continue growth promotion antibiotics, albeit under a different guise. In the Netherlands, initial attempts to curb antibiotic overuse via a ban on growth promotion were not very successful. Only after Dutch authorities and industry sectors ended antibiotic use for both growth promotion and routine disease prevention were they able to achieve overall reductions in antibiotic use in livestock production of more than 60 percent.

Under Recommendation A3, the language under the "Considerations" section urging all countries to employ risk analysis to justify the removal of antimicrobials for growth promotion is unnecessary and unjustified, as well as unsupportable in resource-limited countries. The World Health Organization (WHO), the European Medicines Agency, the U.S. Food and Drug Agency and other national regulators have already expended significant resources marshaling the science and case for ending growth promotion uses. Against that backdrop, there is little scientific or public health rationale for further risk analyses to justify bans on growth promotion, an economic usage of antimicrobials which has no health value. OIE is on record as not supporting the use of antimicrobials for growth promotion, although in other circumstances OIE language carves out an exception for continued growth promotion use where a risk analysis has been done. This exception

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³ See European Parliament legislative resolution of 25 October 2018 on the proposal for a regulation of the European Parliament and of the Council on veterinary medicinal products (COM(2014)0558 – C8-0164/2014 – 2014/0257(COD)), Retrieved from

http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P8-TA-2018-0421+0+DOC+XML+V0//EN&language=EN.. Paragraph 44 of the new legislation states: "Antibiotic medicinal products should not be used for prophylaxis *other than in exceptional cases* only for the administration to an individual animal. Antimicrobial medicinal products should be used for metaphylaxis [disease control] only when the risk of spread of an infection or of an infectious disease in a group of animals is high and where no appropriate alternatives are available."

is unnecessary. For these reasons, we urge the IACG to delete the reference to risk analysis under this recommendation.

In addition, we urge that <u>Recommendation A3</u> could be strengthened with acknowledgment in the Consideration section that the OIE currently calls for antibiotics that are Critically Important, either for humans or animals, to not be used for disease prevention.

Under <u>Recommendation A1</u>, we support the IACG's acknowledgement of the importance of water and waste management from pharmaceutical manufacturing facilities. Improperly managed pharmaceutical waste contributed to downstream spread of antimicrobial residues, drug-resistant bacteria and resistance genes; and, as is already noted, proper management pharmaceutical waste can help reduce that risk. More than 100 pharmaceutical manufacturers and other companies involved with the <u>AMR Industry Alliance</u> also support doing more to reduce such environmental pollution, and its contribution to antimicrobial resistance.

Under <u>Recommendation E1</u>, we support the IACG's call for urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat and for the investment of resources that will permit the Leadership Group to operate effectively.

The IACG's mandate is to provide guidance that can help Member States sustain effective action globally to tackle the health crisis posed by antimicrobial resistance. With these comments, we highlight specific approaches and messages we believe are especially important to the IACG in achieving that mandate.



ReAct - Action on Antibiotic Resistance

Response to the Draft recommendations of the ad hoc Interagency Coordination Group on Antimicrobial Resistance

KEY GENERAL MESSAGES¹

- ➤ We commend IACG on the strong emphasis on affordable and equitable access throughout the recommendations, and the link with the principles from the Political Declaration. There are strong reasons to reiterate the importance that present and future initiatives should follow all the principles already agreed on by the Member States.
- > There is a lack of reflection on the process and the ways forward on how to implement the recommendations. We wish to see a more clear suggestion on who should be responsible to carry forward the recommendations, and more closely link them with global and national mandates and mechanisms for accountability.
- ➤ The relevance and importance of the individual recommendations would benefit from being framed within a larger systems perspective. All recommendations are connected and important for taking action. For example the role of civil society (C1) and how important their contribution to accelerate implementation of National Action Plans (A2).
- ➤ Make the urgency of reacting to the challenge of antimicrobial resistance more prominent in the recommendations. The imminent and already present threat posed by antimicrobial resistance must come across more strongly and that policy makers must urgently act and make it in connection with a pay now or pay much more later argument.
- ➤ Target-setting must be emphasized much more prominently throughout the recommendations. Targets must be set both at the country level and globally. Measurable and achievable milestones will serve as a crucial accountability mechanism.
- ➤ Conflicts of interest must be addressed at all levels of the recommendations, particularly where industry is suggested to play a role or contribute in global governance, financing, and implementing interventions on stewardship or access.
- ➤ The recommendations should more strongly emphasize the need to mainstream AMR into broader agendas on universal health coverage, sustainable development, water and sanitation, infection prevention and control, food production and sustainable environment.

¹ Global discussions on AMR today are often mostly about antibiotic resistance (ABR) even if the AMR term is used more broadly. The AMR vs. ABR distinction should be kept in mind when discussing solutions for ABR because funding strategies and interventions for HIV, malaria and TB can be very different from tackling challenges of ABR in human, animal and environment sectors.



A. ACCELERATE PROGRESS IN COUNTRIES

- Country action as detailed in Recommendation A1 is key for success. However, the efforts listed fall short of being "practical and feasible to implement". Some concrete actions that could be taken as a first step are mentioned instead under considerations and should be lifted up. These include target setting, surveillance and addressing shortages and stock outs.
- Recommendation A2 should present practical and feasible options for supporting countries to implement National Action Plans. There were several proposals that are worth highlighting here, including the ones raised in the IACG Discussion papers on National Action Plans, and on Meeting the Challenge of Antimicrobial Resistance: From Communication to Collective Action. For example:
 - o Support countries with the costing and prioritization of NAP implementation.
 - Provide technical support in different sectors and for example in raising awareness and knowledge, surveillance, stewardship and IPC.
 - o Provide assistance to strengthen national regulatory systems.
 - Map various stakeholders, programs, funding streams for AMR that are accessible for countries.
- In the Considerations of Recommendation A2, a stronger case for target setting and data collection should be made. This could be framed as how essential data is for taking action, both for developing local/national guidelines and policies, increasing accountability and monitoring progress of the response. Building capacity and systems will be essential for country level surveillance of resistance and consumption data. Complementary data collection approaches will be important where there is not yet capacity to develop surveillance systems. Setting measurable targets is an essential accountability and monitoring instrument. There should be targets for access to antibiotics, curbing excessive use, and lowering drug resistance levels.
- A key to action at country level has been the presence of champions and we commend the mention of champions in Recommendation A2, but would like to see their role expanded on in the Considerations. Creating networks of cross-sectoral national experts and champions can drive NAP implementation. These champions need to have the mandate and resources to for example engage stakeholders, build in-country collaborations, mobilize human resources, and ensure accountability.
- Recommendation A3 is good as a first step, but it will be crucial to put in place monitoring systems to make sure use is not just re-labelled from growth promotion to routine prevention. It will also be important to create improved and sustainable animal husbandry conditions as antibiotic use can mask problems of infection control and decrease of antibiotics can have consequences for animal welfare if not addressed. Higher animal welfare is a goal in itself, and will lead to higher productivity and decreased antibiotic use as healthy animals do not need antibiotics.



B. INNOVATE TO SECURE THE FUTURE

- We commend the IACG for reiterating that "all research and development efforts to address antimicrobial resistance should be needs-driven, evidence-based and guided by the principles of affordability, effectiveness, efficiency and equity." However, the principle of delinkage is completely missing from the recommendations, despite being put forth in the UN Political Declaration. The recommendation could specify that all the principles already agreed on by the Member States should be followed.
- Recommendation B1 should more clearly highlight the need for investments and innovation across different areas of research and development. We commend IACG on the last point of the considerations addressing the need to fund a broader research agenda within areas such as implementation and behavior change communication. This should be lifted into the main text of recommendation to highlight the urgency for committed funding within these domains. In relation to this there is a need to make the point that most existing international mechanisms for research and development do not have this specific focus, and that mechanisms for funding this type of research must be made accessible.
- We support the IACG that funding must be mobilized for innovation. However, under considerations for recommendation B1 and B2 a number of existing initiatives in R&D are named for which the IACG "recommends full and sustained funding". As it stands it is unclear on what basis these initiatives have been selected. It would be advisable that a thorough independent analysis is conducted before resources and funding is committed to any specific initiative. A guiding principle could be to direct funding to new or existing initiatives if they follow the principles of being needs-driven, evidence-based and guided by the principles of affordability, effectiveness, efficiency and equity.
- Most current initiatives only cover parts of the drug development pathway.
 Incentives for R&D should focus on the scientific bottleneck of early drug discovery as well as address market and structural barriers to ensure affordable and equitable access to health technologies needed to address AMR.
- The call in recommendation B3 for "undertaking coordinated global mapping of research and development activities" would benefit from being elaborated on in the considerations. Most current efforts to map research efforts are not global, and there is a need for seeking broader inclusion and buy-in from in particular more LMICs in these initiatives. This could also be further expanded on and include a recommendation to develop a coordinated research agenda across the whole spectrum of sectors and disciplines.



C. COLLABORATE FOR MORE EFFECTIVE ACTION

- We commend that the IACG lifts the importance of CSOs and their role, and strongly commend the IACG for lifting the "Provision of political, financial and technical support for civil society organizations to enhance their engagement, including for work with governments" to secure that CSOs can have this important role. CSOs also have an important role in ensuring transparency and accountability in the National Action Plan implementation process, and so the recommendations should push for greater CSO involvement in the implementation of NAPs. It will important to safeguard this support from the global community, as in many countries the role of CSOs has been seriously challenged.
- Conflict of interest and due diligence regarding private sector engagement must be addressed under Recommendation C2. It is of particular concern that the recommendations promote the engagement of the private sector in ensuring access, equity, prudent use and stewardship. The involvement of the pharmaceutical industry in leading activities on prudent use and stewardship is a clear risk of being influenced by conflicting economic interests and marketing. A recent example is the partnering of the Indian Council of Medical Research with Pfizer to form a center that serves as a nodal point to launch pan-India interventions on Surveillance, Stewardship, Advocacy and Awareness, despite numerous evidence of huge conflicts of interest in pharmaceutical companies getting involved in stewardship efforts. The public sector must be in charge of securing access and equity, so it would be important that this role of the public sector is much more prominent in the recommendations.

D. INVEST FOR A SUSTAINABLE RESPONSE

- The structure of the recommendations could more clearly show that investments
 fall into three major categories: already existing funding that goes to AMR;
 applying an AMR lens to existing funding streams and approaches; the need for
 new financing mechanisms.
 - O It is commendable that existing institutions and funds are recommended to give greater priority to AMR in their resource allocations. However, it should be noted that not all areas touched by AMR are covered by existing initiatives and financing streams. Making sure that funding exists for all areas should be a priority. There should be a better allocation of the money and investment into more cost-effective strategies such as IPC and improving health care systems.
 - O Applying an AMR lens to existing initiatives is an important instrument that we agree with. However, for this approach to be effective, there should be a strategy to measure the results and impact of the funding. This should be supported by the availability and transparency of granular information on existing initiatives and funding flows on AMR sensitive workstreams.



- Proposals for how new money also need to be raised to fulfill functions at both global and country levels, not only "relabeling" of existing funds. We have put forward several recommendations for future actions on financing that can be found in a paper published by ReAct and Dag Hammarskjöld Foundation².
- We are lacking a clear message on the urgency to mobilize investments at all levels. More concrete proposals should be made on financial solutions for the near future and longer term.
- The recommendations should more clearly reflect that investments are needed both on national and global levels. On a national level the recommendations should call for Member States to step up their domestic funding efforts for the implementation of National Action Plans. On a global level the recommendations should call for securing finance of the functions required for the global coordination of the response to AMR.
- There is a need to more closely link the considerations to each point of the respective recommendation, especially for D1, so it becomes more specific and concrete. The considerations should elaborate and provide clarity on practical and feasible ways forward on the proposed mechanisms to mobilize funding. South-south cooperation is mentioned but also north-south and triangular cooperation can serve the needs of LMICs. It could also be highlighted that such cooperation will have benefits not only for resource mobilization, but also for capacity building and knowledge sharing.
- Given the push for an increased mandate for the Tripartite, the recommendations should also call for the individual members of it to step up their funding towards AMR work within the Tripartite collaboration. An increased funding commitment by Member States toward the agencies is also needed to support capacity-building and enable technical assistance from the Tripartite to countries. Clear milestones and evaluation strategies should also be established to measure the progress of the Tripartite. If the Tripartite falls short, a larger UN response should be triggered.

E. STRENGTHEN ACCOUNTABILITY AND GLOBAL GOVERNANCE

• Under Recommendation E1, we commend the mention of the Committee on World Food Security (CFS) as a model governance mechanism. The responsibility and decision power of Member States must be emphasized in the proposal for global governance. The composition and operations of the One Health Global Leadership Group should meet the governance functions needed on a global level, including coordination at the intergovernmental level as well as across international agencies and organizations. The primary role of the global governance should be to facilitate national work and allow financing mechanisms

² https://www.reactgroup.org/wp-content/uploads/2018/12/Antimicrobial-resistance-and-sustainable-development-A-planetary-threat-but-a-financing-orphan-ReAct-DHF-December-2018.pdf



- to function properly. The responsibility and decision power of Member States must therefore be emphasized in the proposal for global governance.
- The consideration should bring clarity on how to avoid or manage conflict of interests in all governance structures and multi-stakeholder engagements. In this regard, we oppose SUN as a model governance example as its structure allows for industry interference. There is a need to better clarify the roles, mandates and functions of the different stakeholders in the multi-stakeholder partnership platform, by for example defining decision power and advisory roles of the governance structure.
- We commend IACG on Recommendation E2 to convene an Independent Panel of Evidence for Action against AMR. To ensure that the Panel's work remains independent, its hosting, staffing and funding should not be tied to agencies that might otherwise have a vested interest. The value of this Independent Panel is to remain above, separate and truly independent of any particular intergovernmental agency's efforts, and also focused on AMR-specific concerns.
- We commend IACG on Recommendation E4, on urging the finalization of the process of the Global Stewardship and Development Framework. There should be a clear call for the IACG recommendations to be considered in the Global Stewardship and Development Framework. However, in the first consideration, the IACG notes that "The IACG recommends that priority be given to adopting and implementing global standards and best practices established by the Tripartite agencies (FAO, OIE and WHO) and other international and national authorities, and that the current debates and discussions should not distract from this priority." If focus is only on non-binding options such as sharing best practices, important pathways including legally binding options the Framework could consider may be lost.

RESULTS UK

IACG feedback from RESULTS UK

Respondent: Rachael Hore (Tuberculosis Policy Advocacy Officer) representing feedback from RESULTS UK.

RESULTS UK welcomes the draft recommendations of the Ad Hoc Interagency Coordination Group on antimicrobial resistance (AMR). As recognised in the introductory remarks of the paper, tuberculosis (TB) is a present AMR challenge. Fewer than 20% of all people with multi-drug resistant TB (MDR-TB) worldwide are correctly diagnosed and start treatment which is a major driver of the ongoing MDR-TB epidemic and the global threat of AMR. Drug-resistant TB (DRTB) presents an existing "worst case scenario" for AMR. It is the only drug-resistant infection that is airborne, and is currently responsible for one third of all AMR-related deaths. According to recent research, if global efforts to tackle TB continue at the current rate of progress, from 2015-2030, 28 million people will die, at a global economic cost of US\$ 983 billion. The urgent need for action to address DRTB, as well as draw on the lessons that can be learnt from the experience in DRTB, must be adequately reflected throughout this document. Experiences in DRTB can be a pathfinder for addressing AMR more broadly and the developments for TB will be transferable.

In terms of specific feedback on the recommendations, please see below our feedback for consideration:

Recommendation A1:

- Draw lessons learned from pooled procurement agencies, such as GDF: RESULTS UK welcomes the focus on equitable, affordable access to existing and new quality-assured antibiotics. The pooled procurement mechanisms, such the Global Drug Facility (GDF) for TB and the Global Fund Pooled Procurement Mechanism for HIV, have increased the number of suppliers, allowing the price of essential medical commodities to decrease whilst ensuring that antibiotics are quality-assured, therefore increasing access to treatment. We ask IACG to consider working with forecasting and procurement agencies, such as GDF, to share lessons learned, and to consider expanding the mandate of GDF to include AMR.
- Recognise the impact of countries facing transition from international financing: addressing
 shortages and stock outs, ensuring effective demand forecasts, providing affordable access, and
 leveraging existing pooled procurement mechanisms for access to antimicrobials could all be put
 at risk by the process of transition of procurement activities funded by international financing
 such as Global Fund which facilitate access to pooled procurement mechanisms, to nationally
 negotiated procurement using domestic funds. Provisions to address the particular challenges
 faced by these countries must be addressed.
- Strengthen diagnostic capacities: as well as strengthening prevention measures, countries should also look to strengthen diagnostic capacities. For example, the UN High-Level Meeting on TB Political Declaration committed countries to diagnose and treat 40 million people with TB and 1.5 million people with DRTB by 2022. It is essential that diagnostic capacities for TB and other infectious diseases are strengthened around the world to enhance the ability of countries to diagnose and treat infections including forms of AMR.

Recommendation A2:

• Ensure synergies between National Action Plans on AMR and National Strategic Plans for TB: this recommendation should note the commitment of the 2018 UN High-Level Meeting on TB Political Declaration to "Ensure that TB programmes actively contribute to developing national AMR strategies, capacities and plans and that lessons learned from global, regional and national efforts to combat DRTB inform the design and implementation of both global AMR strategies and national action plans (NAPs) according to national contexts (27)." In recognition that in high

burden TB/DRTB countries, as identified by WHO, the priority drug-resistant pathogen is DRTB, the development and implementation of National Action Plans on AMR and National Strategic Plans for TB must be closely linked, complementary and synergistic.

Recommendation B1:

- Ensure that new products are accessible: RESULTS UK welcomes the recommendation for funders to increase investment for new antimicrobials and would like to ensure that this includes antimicrobial agents that work against TB. In the development of new financial and non-financial market incentives, it is key that these ensure the affordable access to final products and where these investments have been made by public or philanthropic agencies that the results of this research are treated as a "public health goods" and made available to all.
- Include the principle of delinkage, as outlined in the 2016 UN Political Declaration on AMR: RESULTS UK welcomes the reference to the "principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance." We would like this reference to be expanded to include the Political Declaration's acknowledgement of "the importance of delinking the cost of investment in research and development (R&D) on AMR from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools vaccines and other results to be gained through R&D." Any new incentive mechanisms, particularly those using public and philanthropic funding, should promote the delinkage of the costs of R&D from the final price of the product.
- Build on expertise of PDPs: RESULTS UK welcomes the recognition of the important role of Product Development Partnerships. While the recommendation calls for the establishment of more partnerships, the experience and expertise of existing partnerships can also be harnessed to address AMR. This is demonstrated by the expansion of the International AIDS Vaccine Initiative into TB vaccines and AMR R&D, building on the infrastructure and knowledge built up in pursuit of an AIDS vaccine.

Recommendation B2:

• **Include TB:** when setting up any new global initiatives to ensure access to tools to combat AMR, they should include tools that can be used to diagnose, treat and prevent DRTB.

Recommendation B3:

- Facilitate a research enabling environment: RESULTS UK welcomes the call to strengthen research collaboration and promote synergies and opportunities for collaboration. Not only is the development of mapping of R&D activities and funding important to this but also ensuring that there is a research enabling environment created for all areas of AMR R&D. To facilitate this research enabling environment, all funders, particularly public and philanthropic funders should make the data and intellectual property (IP) generated by their research available to all, using data sharing platforms and patent pooling organisations, such as the Medicines Patent Pool. The importance of data and IP sharing is particularly important for TB where combinations of antimicrobials are required to develop successful treatments for DRTB, but equitable access to data and IP may become increasing important for other priority pathogens that may benefit from a combination approach to treatment.
- Welcome the inclusion of TB in the scope of work of the Hub: RESULTS UK welcomes the efforts
 of the Global Antimicrobial Resistance Research and Development Hub, as a concrete outcome of
 G20 commitment and collaboration on AMR, and welcome the commitment by Germany to
 ensure that the Hub's scope of work includes TB.

Recommendation C1:

• Welcome collaboration with civil society and other global health initiatives: RESULTS UK welcomes the promotion of synergies with civil society groups and experiences from other global health initiatives including HIV, TB and malaria to identify synergies and opportunities to achieve shared gains by addressing AMR in their advocacy and programming efforts.

Recommendation D2:

Define the role of Global Fund: RESULTS UK supports the ask of the Global Fund to Fights AIDS,
TB and Malaria to give AMR greater priority in their resource allocations, for example the Global
Fund should claim its role in delivering on the UN High-Level Meeting on TB's Political Declaration
commitment to diagnose and treat 1.5 million people with DRTB by 2022, and reflect this in their
funding allocations. We support the inclusion of MDR-TB in the TB allocation of the Global Fund.

Recommendation E1:

- Ensure representation of TB community in coordination efforts: it is important that the One Health Global Leadership Group on AMR contains a representative from the TB response to ensure that AMR concerns are reflected in the TB response and DRTB remains a focus in the global AMR response.
- Promote synergies between AMR and TB on accountability: the IACG should work together with
 the TB community which has undertaken analyses of accountability mechanisms in preparation
 for the UN High-Level Meeting on TB in 2018 to ensure that the commitments of the Political
 Declaration are delivered on.



SIWI input to the IACG Draft Recommendations

SIWI welcomes the opportunity to provide input to the draft and would like to highlight two aspects:

1. Supporting the role of WASH

SIWI welcomes the strong mention of inadequate access to water, sanitation and hygiene (WASH) among the root causes of antimicrobial resistance (AMR) and strongly supports this being reflected as the very first recommendation A1.a. in the context of reducing the dependency on antimicrobials as well as in the considerations for recommendation D1, regarding funding.

2. Strengthening the demand for sustainably produced antimicrobials

While the usage of antibiotics will always lead to an exposure towards microorganisms that can trigger resistance (thus, underpinning the importance of reducing the dependency on antimicrobials as well as reducing the usage to when they are really needed), the emissions from manufacturing must be avoided. There are fragmented approaches for improving supply chains both within the industry and on the demand side. But the lack of transparency and access to supply chain information, hampers the application of efficient sustainability criteria for regulation, subsidies or procurement of antimicrobials.

SIWI therefore suggests a recommendation for coherent sustainability criteria to promote sustainable production that does not release antimicrobials to the environment. SIWI sees procurement currently as the most dynamic market segment when it comes to developing these criteria, but it should be seen as a pilot area that can inform other segments.

References in the draft:

- Recommendation A1.e mentions waste and water management in manufacturing, with the
 following considerations referring to Good Manufacturing Practice. However, currently GMP
 does not take environmental considerations into account. Also, the considerations following
 recommendation A1 focus on access to and quality of the medicine, including procurement. But
 there is neither further guidance on environmental impacts (in line with above), nor mention of
 procurement even as a tool for promoting sustainable manufacturing.
- Recommendation A2.b., mentioning procurement, should be complemented by guidance on sustainability criteria for procurement. Of particular interest are the synergistic effects of the implementation of the 2030 Agenda, which is of key interest for public procurers and clearly motivates the call for sustainable production as a part of AMR strategies.
- Beyond procurement, the national governance mentioned in recommendation A2.d, should highlight requirements on manufacturers, including regulation. This should also be highlighted in the considerations on the need for cooperation and solidarity (p. 5) with respect to the responsibilities of the demand side incentivizing sustainable production, and of the supply side to provide access to information and implement improved sustainability practices.
- Recommendations B1 and B2 mention waste management tools but do not differentiate between healthcare practice and pollution from the supply chain. Implementation and needed

- incentives differ for both parts and it should be specified that reducing pollution from manufacturing is more than mere waste management.
- Recommendation C2, and especially C2.b highlight private sector responsibility. Again, coherent tools or criteria are necessary, to enable a collaborative approach enabling manufacturers to show improvements and regulators or customers to approve or incentivize these improvements.
- Recommendation D1.d points in the direction of investments in the manufacturing of health products. Be it in investments in production capacity or in purchasing antimicrobials, the sustainability of the supply chain should be a checkpoint in the decision making to avoid emissions of antimicrobials to the environment.

Katarina Veem

Director Swedish Water House and International Policy

Nicolai Schaaf

Programme Manager Swedish Water House

The International Union Against Tuberculosis and Lung Disease (The Union)

IACG feedback from The International Union Against TB and Lung Disease (The Union)

Respondent: Dr Grania Brigden, Deputy Director TB and HIV department representing the feedback from The International Union Against Tuberculosis and Lung Disease. (The Union)

The Union welcomes the draft recommendations of the Ad Hoc Interagency Coordination Group on AMR. The first descriptions of infectious diseases becoming resistant to the anti-microbial treatments were for drugs to treat tuberculosis (TB). Since then Antimicrobial resistance (AMR) is now recognized as a global health threat with glaring economic and social consequences. It is estimated that 100 trillion USD of economic output would be lost due to AMR by 2050. Moreover, TB makes up a substantial portion of the AMR problem with of the 10 million expected AMR deaths in 2050, a quarter will come from DR-TB alone. Tackling DR-TB would be an ideal pathway to highlighting potential solutions to key parts of the AMR problem. The work of the IACG is critical to supporting UN members states in their activities to achieve the commitments they endorsed in the 2018 UN Political Declaration on the Fight against Tuberculosis.

Feedback on the recommendations includes:

Recommendation A1:

- The Union welcomes the focus on equitable, affordable access to existing and new quality-assured antibiotics. The role of national forecasting and pooled procurement mechanisms, like the Global Drug Facility (GDF) has allowed the price of TB medications to decrease whilst ensuring the procurement of quality assured antibiotics for the treatment of DRTB with the corresponding increase in access to DRTB treatment. We ask to IACG consider working with forecasting and procurement agencies like the GDF and to explore expanding the mandate of these organisations into AMR, particularly GDF that currently works with supply and forecasting in TB antimicrobials to share lessons learned with regards to recommendation 1.

Recommendation A2:

For some high burden TB countries, particularly those in the WHO top 30 high burden countries for MDR-TB, it is important that there is close linkages between the development and implementation of AMR action plans and that of the National Strategic plans for TB as for these countries (and potentially others) the priority drug resistant pathogen is drug resistant TB and as such the TB and AMR response should be complementary and synergistic. It is important that both the national strategic plans for AMR and TB are fully financed and do not detract from each other.

Recommendation B1

The Union welcomes the recommendation for funders to increase investment for new antimicrobials, and would like to ensure that this includes antimicrobial agents that work against TB. In the development of new financial and non-financial market incentives, it is key that these ensure the affordable access to final products and where these investments have been made by public or philanthropic agencies that the results of this research are treated as a "public health good" and made available to all. Additionally new incentive mechanisms, particularly those using public and philanthropic funding, should promote the delinkage of the costs of R&D from the final price of the product.

Recommendation B2

- When setting up any new global initiatives to ensure access to tools to combat AMR, these initiatives should include tools that can be used to diagnose, treat and prevent DRTB and consider tools that can be used for a variety of priority pathogens, including TB.

Recommendation B3

- The Union welcomes the call to strengthen research collaboration and promote synergies and opportunities for collaboration. Not only is the development of mapping of R&D activities and funding important to this but also ensuring that there is a research enabling environment created for all areas of AMR R&D. To facilitate this research enabling environment, all funders, particularly public and philanthropic funders should make the data and intellectual property (IP) generated through their supported research available to all, using data sharing platforms and patent pooling organisations, such as the Medicines Patent Pool. The importance of data and IP sharing is particularly important for TB where combinations of antimicrobials are required to develop successful treatments for DRTB, but equitable access to data and IP may become increasing important for other priority pathogens that may benefit from a combination approach to treatment.

Recommendation E1

- It is important that the One Health Global Leadership Group on AMR contains a representative from the TB response to ensure that the AMR concerns are reflected in areas of the TB response as well as ensuring that the importance of DRTB remain a focus in the AMR global response.

Universities Allied for Essential Medicines - Europe (UAEM)

<u>Universities Allied for Essential Medicines (UAEM) response to the public consultation on the draft recommendations of the interagency coordination group on AMR (IACG)</u>

(sent by Sebastian Schönherr on behalf of UAEM) February 2019

General Comments

- We appreciate the work being put into this and are glad that CSOs are part of this process.
- The report is good but could convey more urgency and be more progressive and concrete in its recommendations, as it is not supposed to present status quo but to guide and move things forward.
- How will this set of recommendations and the Global Framework for Development and Stewardship work together, maybe a comment on this could be useful.

Specific Comments

B1

In recommendation B1 the IACG recommends to implement further financial and non-financial incentives targeting important research and development needs. What is meant with non-financial incentives? It should be made clear in the report, that further IP-incentives or transferable exclusivity vouchers should not be considered, as they put affordability and access to new medicines at risk.

We are glad that the principles of the 2016 UN Political Declaration on Antimicrobial Resistance are taken up in this recommendation, yet we wonder why "delinkage", which was stated in the declaration, isn't mentioned in your recommendation as it seems crucial in order to secure affordability.

As a consideration the IACG points out that additional funding as well as incentives are particularly required to bring innovative products from fundamental research to registration, including to accelerate clinical trials. Already at this early stage of research and development equitable access to potential products should be considered. Especially if R&D is publicly funded, as it often is the case in AMR-research. One way to achieve this could be to tie access conditions to all sources of public R&D-funding. Public institutions should follow the model of Global Access Licensing¹ when transferring their intellectual property to private stakeholders.

B2

¹ https://uaem.org/our-work/global-access-licensing-framework/

Under B2 the IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines [...]. This recommendation is crucial, unfortunately it does not convey the sense of urgency that would be appropriate, given that there are still more people are dying of a lack of access than of drug resistance. Further the recommendation is very vague. More concrete points would make it a lot more powerful. The need for new global access initiatives should not only be considered but strongly recommended.

We do agree that existing initiatives should be scaled up. The report lists existing initiatives, yet it is not clear how effective each one of them will actually be at promoting equitable access. While GARDP seems to be a promising and truly innovative initiative some do less so. It appears that CEPI does not have a very strong access policy, partially due to recent changes, as pointed out by MSF². Before committing resources to specific initiatives an independent analysis should be conducted. Funding to initiatives should follow the principles of the UN Political Declaration and be needs-driven, evidence-based and guided by the principles of affordability, effectiveness, efficiency and equity.

There is a particular focus on low income countries. While we fully agree that equitable and affordable access to existing and new antimicrobials is extremely important, we wonder whether this focus on low income countries is limiting since they need to be accessible to everybody and in every country, after all some middle income countries are amongst the ones struggling the most with AMR.

B3

Recommendation B3 calls for research collaboration and in this sense for openness and transparency in data from all research. We highly agree with this point, as to this day still only about half of all clinical trials get published, which is not only wasteful but also unethical. Adherence to WHO-recommendations on clinical trials transparency as outlined in the *Joint statement on public disclosure of results from clinical trials*³ should a be condition tied to all publicly funded R&D. Journal publications should be Open Access to not hinder researchers from accessing them and to therefore further enhance collaboration.

² https://msfaccess.org/msfs-response-cepis-policy-regarding-equitable-access

³ https://www.who.int/ictrp/results/jointstatement/en/



USP Comments on Draft Recommendations of the Ad Hoc Interagency Coordination Group on Antimicrobial Resistance

Submitted by Katherine Bond, Vice President, International Public Policy Advocacy

The US Pharmacopeia (USP), is a 200 year-old nonprofit, public health organization committed to ensuring medical products quality globally. USP sets standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements.

Poor-quality medicines contribute to treatment failure and directly drive pathogen resistance to life-saving treatments such as antibiotics and antimalarials.

Poor-quality antimicrobial medicines are found throughout the world, disproportionately in low and middle income countries with under-resourced regulatory systems. On average, 12.4% of antibiotics and 19.1% of antimalarials are substandard or falsified in low resource settings. Co-endemics of infectious diseases and substandard medicines threaten health security globally.

Poor quality medicines contribute to antimicrobial resistance by:

- 1. Driving the emergence and spread of resistance directly
- 2. Exposing pathogens to sub-therapeutic doses of active ingredient
- 3. Undermining the strategies typically touted for AMR containment

Published and ongoing laboratory research suggests that degraded and substandard medicines for tuberculosis and malaria fuel the emergence and spread of drug resistance and could render current treatments ineffective.

When patients receive sub-therapeutic doses from medicines it has the same effect as not taking the medicine as prescribed. Sub-therapeutic of pathogens creates conditions that enable resistant pathogens to outcompete sensitive ones.

Typically, policymakers target strategies to contain AMR which include stewardship of existing medicines, broad access to affordable medicines, and investment in the development of new antimicrobials. However, if the medicines are not quality-assured, then it is impossible to be a good steward (as this implies getting the right medicine in the right dose to the right patient), and broad access to affordable but poor quality medicines may actually accelerate the emergence and spread of resistance. The strategies assume quality medicines, but quality cannot be assumed, it must be assured.

Unlike other factors driving antimicrobial resistance, there are known solutions to assuring medicines quality.



USP Commends the IACG for recognizing this important driver of AMR in its draft recommendations and has the following comments:

A. Accelerate Progress in Countries

Recommendation A1 emphasizes quality-assured antimicrobials and prudent use in several areas, and explicitly highlights tackling substandard and falsified medical products as a component of ensuring access and stewardship. The recommendation focuses on strengthening surveillance and supply chain mechanisms. We suggest broadening this consideration to strengthen regulatory systems through the medical product lifecycle, including the review of medicines applications for market-authorization, post-market surveillance of antimicrobials and adequate assurance of quality throughout the supply chain. Appropriate use will not be effective if the medicine itself is not quality assured.

Likewise, local manufacturing capabilities will also be strengthened to ensure quality of medicines, especially in the event of shortages. Drug shortages are one of the key risk factors for substandard and falsified medicines entering the market place. Pooled procurement mechanisms should also follow guidelines to assure quality. Such guidelines have been developed and should be encouraged for adoption by countries as well as donor governments.

The recommendation to strengthen national surveillance and regulatory frameworks and enforcement capacity should include explicitly monitoring not only access, availability and affordability, but also quality.

Recommendation A2 includes strengthening key national systems for infection prevention monitoring, integrated surveillance, procurement of health commodities and waste management. Specifically, the emphasis on integrated surveillance and monitoring systems needs to include antimicrobial post-market surveillance as well as pathogen surveillance. Such an integrated system will not only help to identify poor quality medicines in the market and contribute to their removal, but will also provide a better understanding of public health risk in areas where pathogens and poor quality interact and spread resistance.

B. Innovate to Secure the Future

Just as quality assurance needs to be emphasized for existing antimicrobials, it is equally important that it is a factor in research and innovation. We highlight the need to emphasize "new quality-assured health products," driven by the principles of affordability, effectiveness, efficiency, *quality* and equity.



Implementation and operational research, including on mechanisms of transmission of drug resistant infection and implementation of effective approaches should include the "bug-drug dynamic," and provide a stronger base of evidence in order to focus resources in this area.

Global access initiatives should think about quality assurance from the outset in developing R and D strategies and not as an after-thought downstream. New approaches to development and manufacturing require quality standards in order to assure wide access and consistency.

C. Collaborate for More Effective Action

USP welcomes the recommendation to engage civil society groups and organizations as key stakeholders in the One Health response to AMR at all levels. We note that scientific organizations, in addition to professional societies, NGOs, consumer organizations, livelihoods organizations can contribute to responsible stewardship, and commit to bringing our science-based standards, tools, resources and networks to address this global threat. The Medicines We Can Trust Campaign, a global movement advocating for medicines quality by bringing the human impact to light, has a strong focus on AMR.

WaterAid

From: <u>Danielle Zielinski</u>
To: <u>IACG-secretariat</u>

Subject: WaterAid feedback on IACG draft recommendations on AMR

Date: Tuesday, February 19, 2019 17:23:24

Attachments:

To Whom It May Concern:

Please find below the compiled feedback from WaterAid, a nonprofit organization, on the draft recommendations. Any questions or clarifications can be addressed to me:

Respondent name: Danielle Zielinski **Title:** Health and WASH Officer

Affiliation: WaterAid

Comments (organized by section):

A. Accelerate Progress in Countries

- We welcome the inclusion of WASH, IPC and Behaviour Change under Recommendation A1 as necessary prerequisites for reducing the need for antimicrobials. However, we are concerned that the wording of Recommendation A1 does not sufficiently reflect the importance of WASH as a crucial preventive measure. The wording of the headline recommendation implies that the focus of Member States should be on ensuring "affordable access" and "prudent use" of antimicrobials. We would argue that investing in measures such as WASH and IPC is fundamental to reducing infections and reducing the use of antibiotics for treatment.
- We therefore propose a new first headline Recommendation that emphasizes the need for Member States to invest in the necessary prerequisites for preventative health and for health systems so that they do not require the overuse and misuse of antibiotics.
- Propose a more specific reference to WASH in healthcare facilities, schools and for household and community use under Recommendation 1A sub-point a. This is because a generic reference to 'WASH' may imply to many policy-makers and WASH practitioners an emphasis on community WASH investments. While these are essential, institutional WASH (in health care facilities, schools and other public service venues) is currently underemphasized and poorly resourced by many governments and donors. WASH in Healthcare Facilities is especially fundamental to tackling the rise of AMR.
- Propose adding an additional sub-point under Recommendation A2 which specifically calls
 for investment in WASH. Suggest: in countries where WHO/UNICEF JMP data indicates that
 the provision of WASH services in healthcare facilities, schools and for household and
 community use is inadequate, NAPs should include prioritized, funded interventions to
 address this, prioritizing WASH in healthcare settings urgently. This is because
 WHO/UNICEF JMP data clearly shows inadequate provision of WASH in many healthcare and
 other settings in LMICs. Without highlighting and addressing this in NAPs for AMR, all other

- strategies for tackling AMR will be undermined.
- Propose adding a 'Consideration' under Recommendation A2 arguing that, given that AMR knows no borders, High-income countries and multilateral donor agencies should invest
 ODA in supporting LMICs to urgently improve WASH in Healthcare Facilities, since without addressing this, AMR will grow and impact upon High-income countries. This investment would be consistent with the UN Secretary-General's 'call to action' on WASH in Healthcare Facilities and with the WHO and UNICEF-led Global Action Plan on WASH in Healthcare Facilities.

C. Collaborate for More Effective Action

• Propose adding reference to WASH within Recommendation C1 sub-point b, such that it reads: Promoting synergies with consumer and civil society groups active in other sectors, including in WASH, climate change and the environment, responses to HIV, TB and malaria, Universal Health Coverage and other aspects of the SDGs. This is because CSOs and coalitions focused on WASH (for instance, the 'End Water Poverty' coalition and WaterAid's many national partners) can be a significant force for accountability and advocacy for urgent action on AMR, but only if they understand the importance of WASH in preventing infections and reducing use of antibiotics. This will require financial and technical support to CSOs focused on WASH, and a step-change in collaboration between CSOs focused on WASH and those focused on health.

D. Invest for a Sustainable Response

- Propose adding reference to WASH within Recommendation D1 sub-point d, such that it reads: Financial support, grants, loans, credits and insurance for terrestrial and aquatic animals and plants, health, WASH, development, food systems, manufacturing of health products, the environment and other relevant areas. This is because investment of domestic resources and ODA in WASH is absolutely critical to laying the foundations for societies and health systems that can prevent and reduce AMR. In many LMICs, WASH is under-prioritized and under-resourced. The scarce funds that are available are often not used to maximum effect, and WASH in healthcare facilities and schools is often under-prioritized. More than 80% of countries report insufficient financing to meet their national WASH targets. It is estimated that SDG targets 6.1 and 6.2 require a tripling of capital financing to \$114 billion a year, with operating and maintenance costs in addition. WASH represents an average of just 3% of total ODA each year. While WASH is mentioned in within the 'considerations' below Recommendation D1, we argue it should be explicitly included in the recommendation wording itself.
- <u>Propose</u> adding reference to WASH within Recommendation D2, such that it is referred to explicitly alongside "human, animal and plant health, as well as food production and the environment". Though not an IFI, we would also propose inclusion of the **Sanitation and Water for All (SWA) Partnership**, as the primary global partnership for WASH, within this recommendation alongside the references to Gavi, the Global Fund et al.

E. Strengthen Accountability and Global Governance

- We welcome the recommendation to establish a **One Health Global Leadership Group on Antimicrobial Resistance** (Recommendation E1).
- <u>Propose</u> under 'considerations' that the Group should include current or former Ministers of
 Water, Sanitation and Hygiene, and other global leaders or eminent persons representing
 WASH. This will ensure that WASH is incorporated as a crucial element of global dialogue and
 action on AMR, and will also catalyze action by the wider WASH sector.
- Welcome the recommendation to establish an **Independent Panel on Evidence for Action on AMR** (Recommendation E2).
- <u>Propose</u> under 'considerations' that **the Independent Panel should include representation from the WASH sector**. There is currently a dearth of evidence and data related to WASH, and to its impact on AMR. National health systems frequently do not capture data on the status of WASH in Healthcare Facilities, making it difficult for policy-makers and donors to invest at an appropriate level. Stronger evidence on the specific links between WASH and AMR will allow health and WASH practitioners to target and prioritize their interventions more effectively for maximum impact on reducing AMR.

Danielle Zielinski

Health and WASH Officer WaterAid America

WVA/19/doc/10

Brussels, February 2019

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Draft Interagency Coordination Group on Antimicrobial Resistance (IACG) Recommendations for Public Discussion.

The World Veterinary Association (WVA) is the world's largest professional, veterinary association. Representing more than 500,000 veterinarians through 95 veterinary member associations on six continents, the WVA unites and is the common voice of the veterinary profession at a global level. The WVA supports the work of veterinarians in diverse areas of medicine, research, practice, and outreach and is guided by its belief in One Health, which recognizes that humans and animals share the natural environment and create harmony with and for each other.

In this context WVA wishes to underline that in recent years the veterinary profession has taken several steps to promote pharmaceutical stewardship and the responsible use of antimicrobials in animals. In a number of countries (with WVA member organisations) the use of antimicrobials in food animals has gone down considerably and in some countries, a decrease of resistance is becoming visible. WVA looks forward to other health professions joining them and moving forward together in the same direction.

The WVA wishes to commend IACG on the development of the draft recommendations, and is pleased to have the opportunity to give feedback. WVA wishes to offer the following comments:

A. ACCELERATE PROGRESS IN COUNTRIES

WORLD VETERINARY ASSOCIATION (AISBL)

Avenue de Tervueren 12 1040 Brussels, Belgium

T +32 2 533 70 22 E secretariat@worldvet.org www.worldvet.org Recommendation A1: The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health.

This recommendation must be supported by efforts both to reduce the need for antimicrobials and improve access through:

- a. Lowering the prevalence of infection through clean water, sanitation and hygiene;
- b. Decreasing the likelihood of diseases and their spread through delivery of existing vaccines and strengthening infection prevention and control measures;
- c. Ensuring best practices in terrestrial and aquatic animal and plant health, food

production and waste management;

- d. Supporting behaviour change through effective communication and incentives targeted at the public and professionals in human, terrestrial and aquatic animal and plant health, as well as food production and the environment;
- e.Developing national instruments based on international standards for equitable access to and prudent use of existing and new quality-assured antimicrobials in humans, animals, plants and food production, as well as waste and water management in health care, manufacturing and farming-related activities; and
- f. Strengthening national surveillance, regulatory and accountability mechanisms.

WVA agrees with recommendation A1 about equitable and affordable access to antimicrobials. However, concerning "... their prudent use by competent, licensed professionals across human, animal and plant health" WVA is of the opinion that further capacity building efforts are needed. Sufficient numbers of qualified and regulated health professionals, in our case licensed veterinarians, covering all areas where antimicrobials are used, are crucial for achieving prudent use goals.

WVA agrees that in settings where trained prescribers are in short supply, students of veterinary medicine and paraprofessionals may also be trained and authorised to prescribe or administer some antimicrobial agents under the supervision of a licensed veterinarian, however this may not lead to structurally replacing prescribers by paraprofessionals. WVA believes that antimicrobial use in animals should only be under direction of a veterinarian, even if necessity in some cases requires that this be by a paraprofessional under the direction of a veterinarian. "Equitable access" does not mean that antimicrobials for animals can be accessed without veterinary oversight and appropriate regulation. As much as possible the properly educated paraprofessionals should work under the responsibility of and have close communication with the-licensed veterinarian.

Regarding supporting action c, about ensuring best practices in terrestrial and aquatic animal health, WVA would like to suggest including here, similar to point b, -the delivery of existing vaccines and strengthening infection prevention and control measures. More-over WVA strongly recommends adding a similar action point for ensuring best practices in the medical field.

In relation to point f, WVA wishes to underline the importance of transparency in the use of antimicrobials. Record keeping and data collection on the use of antimicrobials, together with qualitative and quantitative data on the occurrence of antimicrobial resistance, are indispensable for identifying future goals and for monitoring the progress made in the achievement of such goals.

Recommendation A2: The IACG calls on all Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs that, at a minimum, include:

- a. Prioritized actions and interventions that are specific to the national context and that are costed and funded, including with adequate domestic resource allocations;
- b. Strengthening key national systems for infection prevention, monitoring, integrated surveillance, procurement of health commodities and waste management;
- c. Technical co-operation, capacity development, research and advocacy components, including support for champions at national and local levels to mobilize action on antimicrobial resistance; and
- d. Effective national coordination, accountability and governance mechanisms.

Concerning Recommendation A2, WVA fully supports the accelerated development and implementation of One Health National AMR Action Plans but wishes to remark that for this task, collaboration between the Member States authorities and private partners is indispensable. Private entities, associations, companies, etc, have to be involved and engaged in the development and implementation of the action plans. Good communication between the public (governmental) and the private partners and vice versa needs to be assured.

Recommendation A3: The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins).

WVA agrees with the Recommendation to phase out the use of antimicrobials as growth promoters in food producing animals. WVA also agrees with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (WHO list) as growth promoters

WVA notes that in the OIE third annual report on the use of antimicrobial agents intended for use in animals (2019) no countries reported the use of glycopeptides, ketolides or cephalosporins of any generation for growth promotion.

WVA would also like to suggest complementing this action by setting strict conditions for the use of the Highest Priority Critically Important Antibiotic Agents (WHO list) for therapeutic use in animals and people. Given the importance of this category of antimicrobials they should only be used when no proper alternative treatment is available. Similar to the WHO <u>Guidelines</u> on the use of medically important antimicrobials in food-producing animals, guidelines for a restricted use in people could be developed. Complementing actions in the medical and veterinary field will create a synergistic effect.

WVA supports the IACG statement that "It is particularly important that all countries employ appropriate risk analysis - the process of hazard identification and risk assessment, management and communication - as described in the OIE Terrestrial Animal and Aquatic Animal Health Codes. Such risk analyses should be unbiased assessments that transparently present the evidence base for findings and recommendations and be subject to peer review". WVA believes that the availability of high quality peer reviewed risk analyses will enable improved ability to set priorities and manage risks.

B. INNOVATE TO SECURE THE FUTURE

Recommendation B1: The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials - particularly antibiotics, as well as new diagnostics, vaccines, waste management tools, and safe and effective alternatives to

antimicrobials - for human, terrestrial and aquatic animal and plant health through:

- a. Financial and non-financial incentives strategically targeting the most important research and development needs, scientific challenges, and market barriers based on the principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance; and
- b. Building upon existing Product Development Partnerships in human health and establishing more of them, particularly for terrestrial and aquatic animal and plant health.

WVA agrees with the recommendation to "increase investment and innovation in new antimicrobials - particularly antibiotics, as well as diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials" but we also believe that certainly on the animal health side research into good husbandry practices (biosecurity, animal resilience, herd health plans) is as important as searching for new antimicrobials or alternative treatments.

We estimate that more can be gained by keeping animals under proper conditions they can cope with and that require less medical interventions than through new antimicrobials. Disease prevention through good husbandry and animal welfare practices is also likely to be more sustainable than new antimicrobials which will trigger new resistance mechanisms.

Recommendation B2: The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

WVA wishes to add that an important factor related to "access to existing and new antimicrobials" is assurance that the antimicrobials are of high quality and are used correctly. Recent publications from the OIE show that several countries do not yet have complete and relevant legislation and/or accompanying compliance programmes to ensure appropriate conditions for the import, manufacturing, distribution and use of veterinary medicinal products, including antimicrobial agents. As a result, substandard or falsified agents may circulate and create conditions of high risk for the development and spread of resistance.

Recommendation B3: The IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context by:

- a. Undertaking coordinated global mapping of research and development activities and funding to address antimicrobial resistance;
- b. Establishing and maintaining a platform for sharing information on research and compounds in development in both ongoing and completed research and development activities;
- c. Promoting synergies and opportunities for collaboration among funders and researchers in human, animal and plant health, and the environment; and
- d. Promoting openness and transparency in data from all research and monitoring and surveillance sources.

No comments to recommendation B3.

C. COLLABORATE FOR MORE EFFECTIVE ACTION

Recommendation C1: The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels through:

- a. Strengthening their roles in accountability, advocacy, monitoring progress and ensuring prudent use of antimicrobials;
- b. Promoting synergies with consumer and civil society groups active in other sectors, including in climate change and the environment, responses to HIV, TB and malaria, Universal Health Coverage and other aspects of the SDGs; and
- c. Provision of political, financial and technical support for civil society organizations to enhance their engagement, including for work with governments.

WVA agrees. No further comments.

Recommendation C2: The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels in order to ensure:

- a. Affordable access, prudent use and stewardship of antimicrobials;
- b. Ethical production, distribution and marketing practices, including through environmentally sustainable production and waste management and the elimination of inappropriate incentives to sell antimicrobials;
- c.Engagement by the private sector in collaborative efforts to collect, analyze and use data and realign economic incentives to improve production, distribution and marketing practices; and
- a. d. Contributions to addressing antimicrobial resistance through testing of innovative approaches, corporate social responsibility, and similar initiatives.

See our comments under Recommendation A2.

D. INVEST FOR A SUSTAINABLE RESPONSE

Recommendation D1: The IACG calls upon governments and global, regional, national, bilateral and multilateral financing and development institutions and banks to systematically apply an antimicrobial resistance mitigation and One Health "lens" when making investments through:

- a. Official Development Assistance;
- b. South-South cooperation;
- c. The International Development Association (IDA) replenishment process from IDA19 onwards;
- d. Financial support, grants, loans, credits and insurance for terrestrial and aquatic animals and

plants, health, development, food systems, manufacturing of health products, the environment and other relevant areas.

No comments.

Recommendation D2: The IACG emphasizes the need for increased investment in the global response to antimicrobial resistance. It urges existing and future financing mechanisms in human, animal and plant health, as well as food production and the environment - including Gavi – the Vaccine Alliance, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Global Financing Facility, Multilateral Climate Funds, Unitaid, as well as future financing streams for Universal Health Coverage and other priority development issues, and their donors - to give antimicrobial resistance mitigation greater priority in their resource allocations. It further calls upon public, private and philanthropic donors in human, animal and plant health, as well as food production and the environment, to increase funding to contribute to addressing antimicrobial resistance, including to support implementation of National Antimicrobial Resistance Action Plans.

No comments.

E. STRENGHTEN GLOBAL ACCOUNTABILITY AND GOVERNANCE

Recommendation E1: The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat, to:

- a. Maintain urgency, public support, political momentum and visibility of the antimicrobial resistance challenge on the global agenda, and set targets;
- b. Advocate for action, including support for the expanding work of the Tripartite agencies (FAO, OIE and WHO), UN Environment (UNEP) and other international and regional entities;
- c. Monitor and report on progress, gaps and accountability in the global response to antimicrobial resistance;
- d. Expand multi-stakeholder engagement by establishing a partnership platform with the participation of Member States, UN agencies, international and intergovernmental organisations and regional entities, civil society, the private sector, researchers and other key stakeholders to develop and work towards a shared global vision and coordinated action on antimicrobial resistance;
- e.Provide advice and guidance on reports of the Independent Panel on Evidence for Action against Antimicrobial Resistance (recommendation E2);
- f. Monitor and advocate for the inclusion of antimicrobial resistance mitigation and a One Health "lens" in investments and programmes of major financing instruments for agriculture, health, development, food production and other relevant areas (recommendation D1);
- g.Identify priorities for research and development and facilitate implementation research in a One Health context; and
- h. Define the financial needs and gaps for the global response to antimicrobial resistance, including the costs of inaction and anticipated returns on investment.

The WVA has difficulties understanding the governance structure where-in the proposed One Health Global Leadership Group will function. What will be the mandate of the Group, who are its members,

who do they represent, to whom the Group will report, to whom will the Group be accountable, etc. etc. As long as such questions are not clearly answered there will be a considerable risk that the proposed Leadership Group would operate in parallel with existing structures, which could lead to overlapping activities and undue competition.

Recommendation E2: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.

See our comments on recommendation E1.

Recommendation E3: The IACG requests the Tripartite agencies (FAO, OIE and WHO) together with UNEP and other UN agencies, in the context of UN reform, to further strengthen joint One Health action, based on country priorities and needs, by enhancing their organizational capacity and providing adequate and sustainable core funding for antimicrobial resistance-related activities in order to:

- a.Integrate antimicrobial resistance-related activities into country UN Development Assistance Frameworks;
- b. Provide and update effective normative guidance, standards and tools when needed;
- c. Advise on priority evidence-based interventions and actions;
- d. Provide coordinated technical co-operation and capacity building, including One Health regional platforms for technical co-operation; and
- e.Guide, support, monitor and evaluate implementation, including on infection prevention, integrated surveillance, data quality and harmonization, risk assessment, and demand forecasting and supply management.

No comments.

Recommendation E4: The IACG recognizes the ongoing process led by Member States to develop the *Global Development and Stewardship Framework to Combat Antimicrobial Resistance* and urges the Tripartite agencies (FAO, OIE and WHO) and UNEP to expedite its development in line with the scope described in the 2015 World Health Assembly resolution on antimicrobial resistance (WHA68.7). As Member States finalize this process, they should also consider the need for new international instruments.

No comments.



Draft Recommendations of the Ad Hoc Interagency Coordination Group on Antimicrobial Resistance – Public Discussion Paper

The AMR Industry Alliance welcomes the IACG public consultation as it considers that the health industry is a key stakeholder in the fight against AMR. The comments in this paper represent the AMR Industry Alliance members which gather a wide range of companies from different life-sciences industry sub-sectors (Biotechs, Diagnostics, Generics, R&D manufacturers).

1. General Comments

- The life-sciences industry should be recognized as a true and equal partner in any new AMR governance mechanism. Given that a sustainable solution to AMR will require a coordinated response from all stakeholders, the private sector should also be represented on the One Health Global Leadership Group. Recognizing the key role of the private sector, the draft recommendations could further highlight how much the healthcare industry actions can complement and strengthen public and governmental programs at both local and global levels.
- The draft recommendations should further delineate roles and responsibilities to ensure its
 recommendations can be actionable and that a monitoring and accountability mechanism can be put in
 place.
- The draft recommendations should focus more on interventions that can be implemented in the short term rather than mostly look at potential initiatives for the longer term. This approach would be better suited to the "urgency" of the AMR crisis.
 - For example, the recommendations should further emphasize the role that existing tools, particularly infection prevention practices, diagnostics and stewardship, have in reducing the inappropriate use of existing medicines.
- Further emphasis on the economic impact of AMR and the inclusion of positive incentives to act could help the recommendations get more traction with national governments.
- We recommend highlighting **the need for both "push" and "pull" incentives** in Section B, highlighting the commitments already made by the previous three G20 statements.
- The draft recommendations should **adopt a more holistic approach to improving access** which would systematically link it to the need for better stewardship.
 - i. Strengthening health system capacities is key to improve access to antimicrobials consistently with rational use guidelines. The increased availability of low-priced newer antibiotics could accelerate the development of AMR, especially if deployed in weak health systems with limited capacity to deliver care.
 - ii. A focus on simply increasing access to antibiotics will also contribute to AMR if the production processes are not sustainable.



2. Specific comments on the draft paper

A) Detailed feedback on section B: Innovate to secure the future

- The recommendations in Section B focus primarily on the need for "push" incentives which encourage early-stage research and development. "Pull" mechanisms that ensure a robust and sustainable market for both existing and future innovations are not directly emphasized. Market reforms that ensure both existing and future antimicrobials, diagnostics, vaccines and infection prevention and control tools are available and used will be required. We recommend highlighting the need for both "push" and "pull" incentives in Section B.
- It is our view that Section B, in focusing primarily on the need for future innovations and developments, overlooks the potential for existing tools, especially diagnostics and infection prevention, to minimize the inappropriate use of antimicrobials and extend their useful life. Such solutions are already on the market, while further innovations will take time to access the market.
 - One of the main barriers to adoption is that existing tools are often considered as too expensive or as an additional cost. In many cases, the diagnostic is more expensive than the antimicrobial leading to underuse of diagnostics while overusing antimicrobials. From an economic standpoint, diagnostics and infection prevention programs help save money in the entire healthcare chain.
 - o In this context, we suggest that the IACG final recommendation paper includes a specific recommendation about securing innovation and market access for in vitro diagnostics. Such recommendation could be as follows:

"In vitro diagnostics should benefit from specific innovation and market access mechanisms in order to boost R&D and market access. Such mechanisms could include:

Innovation:

• New evidence-based studies should be designed to reflect the value of diagnostics, when used alone or in combination with other health products and technologies. The value of diagnostics through evidence-based studies on a local and global basis has to be assessed.

Market access:

• Reimbursement practices need to be aligned with public health goals to drive more timely and accurate diagnosis of infectious diseases and incentivize prudent use of antimicrobials. In particular, modification of reimbursement systems to incentivize appropriate diagnostic testing and emphasize prudent antimicrobial use would be critical. The development of member states regulations where antimicrobials should not be prescribed without a diagnostic test would be desirable.



Usage:

• Antimicrobial stewardship programs which emphasize diagnostic stewardship and the prudent use of antimicrobials without compromising patient care are key to combat AMR. Embedding the use of diagnostic tests into prescribing practices in order to decrease reliance on empiric use and emphasize treatment optimization is ideal.

Prescriber performance in employing diagnostics, as appropriate, should be measured and reported to establish a baseline from which progress can be ascertained.

- Strengthen initiatives to boost national, regional, and local laboratory capacity so that there is enhanced access to diagnostic tests and testing facilities in all countries as well as a robust source of reliable data for surveillance.
- Provide support to resource-limited settings and health care facilities on training and education for infection prevention, control, microbiology and antimicrobial stewardship programs.
- In animal health, harmonize diagnostics regulation in order to ensure the same quality level, limit registration fees, and reduce overall development costs."

B) Comments on specific parts of the draft recommendations paper

Page, column,	"Specific Text" from the draft paper	Comment/Suggested Edit	Importance
paragraph			L, M, H
p. 2 (page 3)	"The economic costs of inaction against antimicrobial resistance will also grow. The total annual shortfall in gross domestic product (GDP) due to antimicrobial resistance could be as high as \$3.4 trillion by 2030, equivalent to the losses experienced during the 2008 global financial crisis."	All these economic costs point to the importance of further investments in these areas – we suggest mentioning and linking to finance action below.	Н



p. 2 (page 3)	"Production and supply chains for existing antimicrobials are also vulnerable, with very few producers, leading to shortages of key antimicrobials around the world. As a result, people presenting in health care facilities with drug-resistant infections cannot be effectively treated."	This statement does not acknowledge the underlying cause of these shortages: the low value placed on antimicrobials and the constant pressure on prices which have led to an unsustainable commercial marketplace and contributed to causing manufacturers to exit this space, a situation that would not be remedied by increasing the number of suppliers.	Н
		Suggested edit (in bold): "Production and supply chains for existing antimicrobials are also vulnerable, with very few producers due to an unsustainable market and narrow procurement practices, leading to shortages of key antimicrobials around the world. As a result, people presenting in health care facilities with drug-resistant infections cannot be effectively treated."	
p. 3 (page 4), Recommendation A1 box	[bullet points on improving access]	We suggest adding "Enhance recognition of overall value of antibiotics, vaccines, diagnostics, etc." We propose to clarify in Recommendation A1 what the term "antimicrobials" refers to, as it has in the B1 recommendation: "particularly antimicrobials, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials". For example, suggest for Recommendation A1 to read: "The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials, diagnostics and vaccines and their prudent use by competent, licensed professionals across human, animal and plant health" We also propose emphasizing infection prevention, infection control and prudent use of antimicrobials when discussing the role of surveillance systems. In sub-bullet four of considerations for Recommendation A1, we recommend the discussion of surveillance systems to read as follows (additions in bold):	M



		"Surveillance systems should include specific indicators to enable monitoring of infections, antimicrobial resistance and access, prudent and appropriate use, availability and affordability of antimicrobials."	
p. 4 (page 5), bullet point no. 2 on "Considerations for this recommendation (A1)"	"The IACG emphasizes that ensuring equitable and affordable access to and stewardship of existing and new quality-assured drugs, diagnostics and vaccines is essential for effective national responses to antimicrobial resistance."	While access to new medicines is critical, the evidence shows that it is the lack of access to generics that causes a higher death burden. These drugs are very cheap which suggest that the main barriers to "affordable access to and stewardship of existing and new quality-assured drugs, diagnostics and vaccines" are weak health care systems and in particular deficiencies in financing.	M
		Suggested edits (in bold): "The IACG emphasizes that ensuring equitable and affordable access to and stewardship of existing and new quality-assured drugs, diagnostics and vaccines is a function of effective health systems and is essential for effective national responses to antimicrobial resistance."	
p. 4 (page 5), bullet point on "Addressing shortages and stockouts"	"Governments should establish national drug, vaccine and diagnostics shortage notification systems to allow them to take rapid action in relation to shortages and stockouts of these health products. WHO and OIE should provide guidance to countries on developing or improving existing national drug and vaccine shortage notification systems for human and animal health that are harmonized and employ the same definitions, approaches and	Notification systems do not get to the root cause of potential shortages. Governments need to get to the core of the issue in their respective markets - e.g., weak supply chains and health management information systems, poor forecasting, procurement systems that reward rock-bottom pricing over other factors such as ability to supply; as well as winner takes all tenders which can eventually push competitors (and thus potential supply-gap fillers) out of the market.	Н
	methodologies, where appropriate."	Suggest addition: These systems should be complemented with investments in supply chain strengthening and health information systems that enable countries to better understand and manage the supply of health products and take action to prevent and address shortages and stockouts.	



p. 4 (page 5), bulet point on "Effective national-level antibiotic demand forecasts"	"Improved forecasting is needed in both human and animal health to improve access to antibiotics and to strengthen procurement and supply chain management. This will in turn support efforts by WHO and OIE to develop a global demand forecast model for antibiotics that can be shared with manufacturers and procurement agencies on a regular basis and made publicly available."	While improved forecasting is needed, there is limited value in WHO and OIE developing global demand forecast models for antibiotics: there are no global funders of antibiotic procurement, procurement is decentralized and fragmented across public and private sectors, and there are major data gaps in the use of antimicrobials. Any global forecast by WHO and OIE would be subject to important uncertainty and would have no link to actual planned procurement, making it meaningless for supply planning. Suggested edit: "Improved forecasting is needed in both human and animal health to improve access to antibiotics and to strengthen procurement and supply	Н
		improve access to antibiotics and to strengthen procurement and supply chain management. This will in turn support efforts by WHO and OIE to develop a global demand forecast model for antibiotics that can be shared with manufacturers and procurement agencies on a regular basis and made publicly available."	
p. 4 (page 5), bullet point on "Establishing antimicrobial production facilities"	"Some governments or regional entities may consider establishing production facilities or contracting manufacturers to help mitigate shortages and ensure a resilient supply of antimicrobials, particularly antibiotics and vaccines for human and animal health, paying due consideration to manufacturing standards and quality assurance for health commodities."	Antibiotic manufacturing is complex and requires a long lead-time, as well as highly technical personnel and appropriate facilities. It is therefore unlikely that governments or regional entities can mitigate shortages by establishing small-scale production facilities, especially not in the short term. Construction of new facilities by local governments may not be advisable as this will require a substantial amount of investment and expertise and will not bring an answer to the current issue on concentrations in the supply chain for antibiotic product. The API supply is concentrated due to commoditized market, and when you opt for public and local individual manufacturing the problem may worsen and drive each country to generate its own capacity as private industry would further back away from this production. Finally, this recommendation could produce unintended negative consequences such as the further fragmentation of the generic antibiotic market or the development of "localisation"	Н



		agendas" which could further exacerbate shortages. A proliferation of production centres may also complicate quality control and manufacturing issues from a regulatory point of view. Suggested edit (in bold): "Some governments or regional entities may consider establishing production facilities or contracting manufacturers to help mitigate shortages and ensure a resilient supply of older antimicrobials at high risk of shortages/stockouts, particularly antibiotics and vaccines for human and animal health, paying due consideration to manufacturing standards and quality assurance for health commodities."	
p. 4 (page 5), bullet point on "Providing affordable access"	"Governments should establish policies, measures and mechanisms to provide existing and new drugs, diagnostics and vaccines at affordable prices, including to people who are unable to pay for them."	We cannot win the fight against AMR without properly financed and functioning health systems. The evidence shows that it is the lack of access to generics that causes a higher death burden. Because generic first line antibiotics are already very cheap, the key barrier is a weak health care system, not high prices. Suggested edit (in bold): "Governments should establish policies, measures and mechanisms to provide existing and new drugs, diagnostics and vaccines at affordable prices, including to people who are unable to pay for them. These efforts should prioritize those antibiotics in the as "Access" category of the WHO EML."	M
p. 4 (page 5), bullet point on "Pooled procurement mechanisms"	"Leveraging existing pooled procurement mechanisms in human health and potentially establishing them for animal health could help to secure both the supply of quality-assured medicines and ensure predictability of demand for manufacturers."	Pooled procurement should be used with caution and can only focus on elements of security of supply, not on getting the lowest-price possible, as such would further erode a market that already struggles to supply. Pooled procurement mechanisms will only work for antibiotics if there is an alignment in all participating countries treatment guidelines and regulatory files to allow a level playing field for all manufacturers able to supply. Furthermore, these mechanisms must allow and incentivize for several manufacturers to supply in order to reduce dependence of a single manufacturer and to increase the robustness of the supply chain.	Н



p. 4 (page 5), bullet point on "Tackling substandard and falsified medical	"Tackling substandard and falsified medical products is an important component of ensuring access to quality antimicrobials, including stewardship. Complementary efforts to improve antimicrobial resistance surveillance and supply chain mechanisms - including the	The importance of quality, supporting health infrastructure more broadly should be more strongly stressed. We cannot win the fight against AMR without properly financed and functioning health systems. The importance of supporting higher vaccination rates through various	Н
products"	implementation of low-cost technologies and track-and-trace systems - could help to address this problem in low-and middle-income countries. Furthermore, efforts to ensure Universal Health Coverage also promote access to quality-assured and appropriate use of antimicrobials and play a role in reducing the development of antimicrobial resistance."	programs should also be recognized.	
p. 4 (page 5), bullet point no.5 on "Considerations for this recommendation (A1)"	" requires appropriate attention to and investment in training, accreditation and regulation of professionals, including physicians, pharmacists, veterinarians and other specialists across human, terrestrial and aquatic animal and plant health, as well as in food production and the environment."	We suggest adding dentists, as they are not in the bucket of HCP specialists. Alternatively, we suggest using the term "health care providers".	L



p. 5 (page 6), Recommendation A2 box	[On surveillance]	The IACG recommendations should be more pragmatic on the surveillance question. To make surveillance become a reality, it could highlight the importance of utilizing data from private programs managed by private pharmaceutical and diagnostic companies with public, governmental programs. It could also propose to expand lab capacities while forecasting their transformation into routine testing labs in case of emergency situations, training of local health workers and stakeholders, as well as collection of reliable in vitro data.	M
p. 6 (page 7), bullet point no. 5 on "Considerations for this recommendation (A2)"	"The IACG emphasizes that One Health integrated surveillance and monitoring systems need to be established, coordinated and integrated, covering human, terrestrial and aquatic animal and plant health, food production and the environment. To the extent possible, they should also provide harmonized or equivalent data that can be easily compared, exchanged, used and aggregated locally, nationally and globally. Building on recent efforts, the Tripartite agencies - working together with Member States and other organizations - need to develop and monitor core indicators that cut across human, animal, plant, food and environmental health."	This bullet point would fit better under A1.	L
p. 7 (page 8), B "Innovate to secure the future" section	[Aim of the recommendations in this section]	The importance of driving end-to-end research should be recognized. In addition we commend the IACG for acknowledging the need to incentivize all antimicrobial R&D, including diagnostics, vaccines and alternatives therapies.	M



p. 7 (page 8), Recommendation B1 box	a) Financial and non-financial incentives strategically targeting the most important research and development needs, scientific challenges, and market barriers based on the principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance;	The Political Declaration was rather non-specific. We highly recommend including more specificity about implementing as relevant de-coupled pull incentives, push incentives, and reimbursement reform to support a sustainable ecosystem. Key principles when developing policies to incentivize antimicrobial R&D: There is no one-size-fits-all solution Clear definitions for products that would earn a pull reward are needed Market-based models should be retained to allocate limited resources and reward successful innovation Predictable and sustainable funding is critical The societal value of antimicrobials (antibiotics and vaccines as well as diagnostics) should be reflected in the incentive mechanism The impact of the incentive must be sufficient to support sustainable investment in R&D Reduce and partially decouple the proportion of manufacturer revenue that is derived from antibiotic sales volume Align with stewardship principles that support global access Incentives should include provisions to help mitigate the delay of	H
p. 7 (page 8), bullet point no. 1 on "Considerations for this recommendation (B1)"	"The IACG notes that the unclear market potential for antibiotics, diagnostics and vaccines discourages innovation, primarily due to the high cost of research and development and low success rates for new compounds, as well as uncertainty of revenue in terms of price and volume of new products. Accordingly, additional, sustained investments and collaborations are needed on	the market entry by other generic drugs These aspects are as much true for innovative antibiotics as they are for existing and widely used products. The elements of uncertainty also apply to manufacturers trying to bring off-patent products to the market and thus, create a barrier to the entry of new players to strengthen supplychains. We suggest including incentives in this first bullet point – these are	H
	the part of governments, the private sector and civil society to accelerate research and development, pull new products through to market and ensure effective stewardship."	needed to drive private investment.	



	"The IACG notes that the unclear market potential for antibiotics, diagnostics and vaccines discourages innovation,"	The problem is not that the market potential is "unclear," but that there the market potential is "severely limited." It is this limited potential that is driving disinvestment from antimicrobial innovation, not a clear understanding of the market potential. Suggest replacing "unclear" with "severely limited." Suggested edit: change from "unclear" to "severely limited"	Н
	" low success rates for new compounds, as well as uncertainty of revenue in terms of price and volume of new products."	This part is not about uncertainty, as even with certainty, if the levels are too low, investment in this space can't compete with other areas. It is the known low level market potential. Suggest the part reflect this. Suggested edit (in bold): "low success rates for new compounds, as well as significant economic challenges and limited of-revenue due to low price and volume of new products."	М
	"Accordingly, additional, sustained investments and collaborations are needed on the part of governments,"	It's not just about more 'investment'; stakeholders must also be willing to explore innovative new commercial/market models. We suggest that this be recognized.	М
p. 7 (page 8), bullet point no. 3 on "Considerations for this recommendation (B1)"	"The IACG recognizes the need to develop and provide financial and non-financial market incentives"	We suggest emphasizing the need for predictable and sustainable incentives. These incentives should also be considered for manufacturers looking at improving the reliability of their supply chain and therefore the supply of antibiotics.	M



	"and appropriately targeted to address bottlenecks and market barriers across the product life cycle from fundamental research to registration and equitable and affordable access and stewardship."	Is this meant as "aligned to the principles of equitable"? Suggested edit: "equitable and affordable" to just "equitable", to avoid repetitiveness. Suggested edit (in bold): "and appropriately targeted to all relevant partners (governments, donors, private sector, multilaterals) with a role to address bottlenecks and market barriers across the product life cycle from fundamental research to registration and equitable and affordable access and stewardship."	Н
		We suggest pointing out the need to more appropriately value antibiotics and improve reimbursement to stabilize current market.	Н
p. 7 (page 8), bullet point no. 4 on "Considerations for this recommendation (B1)"	" and the Coalition for Epidemic Preparedness Innovations (CEPI)."	While a very important partnership that is focused on addressing emerging epidemics, CEPI is not focused on AMR and the pathogens it has prioritized are not impactful on AMR – the relevance is unclear.	L



p. 8 (page 9), bullet point no. 5 on "Considerations for this recommendation (B1)"	"The IACG underlines that additional funding combined with financial and non-financial incentives is particularly required to bring innovative products from fundamental research to registration and implementation, including to accelerate clinical trials in humans and experimental work in animals and plants, and to enhance the role of small and medium enterprises in research and development."	The importance of attracting, and maintaining, venture capital will support the engagement of both SMEs and large biopharmaceutical companies. Suggested edit (in bold): "The IACG underlines that additional funding combined with financial and non-financial incentives is particularly required to bring innovative products from fundamental research to registration and implementation, including to accelerate clinical trials in humans and experimental work in animals and plants, and-to enhance the role of small and medium enterprises in research and development, and to create a sustainable innovation ecosystem that supports private investment in antimicrobial R&D."	M
p. 8 (page 9) , Recommendation B2 box	"The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health."	Suggested edit, as above: "equitable and affordable" to just "equitable", to avoid repetitiveness. We strongly suggest linking access to stewardship and a sustainable public health infrastructure.	М
p. 8 (page 9), bullet point no. 2 on "Considerations for this recommendation (B2)"	"The IACG therefore emphasizes the need to leverage existing global access and scale-up initiatives in human health (e.g. CEPI, Gavi, Global Fund to Fight AIDS, Tuberculosis and Malaria, Medicine Patent Pool, Unitaid) wherever possible to ensure access to existing and new antimicrobials, diagnostics and vaccines to address antimicrobial resistance."	The market and access challenges for antibiotics are different when compared to other therapeutic areas like vaccines and HIV, TB, and malaria: there are no vertical programs at the country level to support appropriate use, there are no global funders/procurers, there is significant use of antibiotics in the private sector, important investments are needed in health systems to deliver antibiotics appropriately, there are major gaps in access to older off patent antibiotics. While there may be opportunities to leverage lessons learned and build on the achievements of existing global access initiatives, these efforts should reflect the specific access challenges for antibiotics. Suggested edit (in bold):	H



	words and the governments	AMR with concrete and rapidly actionable initiatives.	
	including working with governments.	private sector has already made and continues to make in addressing	
	engagement of these stakeholders to optimize their contributions to the response to antimicrobial resistance,	This text unnecessarily calls into question the contribution that the	
	recommendations aim to strengthen the systematic	antimicrobial resistance, including working with governments."	
	and the private sector in the response is inadequate. These	and the private sector to optimize their contributions to the response to	
С	antimicrobial resistance, the engagement of civil society	strengthen the systematic engagement of these stakeholders civil society	
Action", Section	essential to tackle the many challenges posed by	sector in the response is inadequate. These recommendations aim to	
More Effective	While multisectoral efforts involving all stakeholders are	antimicrobial resistance, the engagement of civil society and the private	
"Collaborate For		all stakeholders are essential to tackle the many challenges posed by	
p. 10 (page 11),	[Aim of the recommendations in this section]	Proposed change (addition in bold): "While multisectoral efforts involving	Н
		health, including for low-income countries."	
		alternatives to antibiotics in terrestrial and aquatic animal and plant	
		diagnostics, vaccines, waste management tools and safe and effective	
		access to and appropriate use of existing and new antimicrobials,	
(B2)"		"The IACG recognizes the need to develop new global initiatives to ensure	
recommendation	for low-income countries."	Suggested edit (in bold):	
for this	terrestrial and aquatic animal and plant health, including		
"Considerations	tools and safe and effective alternatives to antibiotics in	implementation of strengthened stewardship initiatives.	
on	antimicrobials, diagnostics, vaccines, waste management	society and the private health care sector should partner to support	
bullet point no. 2	initiatives to ensure access to existing and new	importance of stewardship. Member states in partnership with civil	
p. 8 (page 9),	"The IACG recognizes the need to develop new global	We strongly recommend that a new bullet be added that emphasizes the	Н
		alternative therapies."	
		resistance. These efforts should reflect the specific access barriers identified for existing and new antimicrobials, vaccines, diagnostics, and	
		antimicrobials, diagnostics and vaccines to address antimicrobial	
		Unitaid) wherever possible to ensure access to existing and new	
		Fund to Fight AIDS, Tuberculosis and Malaria, Medicine Patent Pool,	
		access and scale-up initiatives in human health (e.g. CEPI, Gavi, Global	
		"The IACG therefore emphasizes the need to leverage existing global	



p. 10 (page 11), bullet point no. 1 on "Considerations for this recommendation (C1)"	"The IACG emphasizes that closer engagement of civil society is essential to advance efforts against antimicrobial resistance at global, regional, national and local levels. This includes medical, veterinary and other professional societies, non-governmental and community-based organizations, consumer rights protection groups, associations of farmers, trade unions, food sector federations, and health and environmental advocates and service providers."	We suggest adding patient organizations. This is a key gap in terms of raising awareness and driving action on AMR.	H
p. 11 (page 12), Recommendation C2 box	The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels in order to ensure:	Due to these being complicated issues which not one policy and/or stakeholder can "ensure", would suggest changing to "strongly support", or "work towards". In this particular matter, the entire healthcare industry plays a key role. Many healthcare companies consider as part of their mission raising awareness about antimicrobial resistance. They support the WAAW, organize health campaigns, conferences, events and other activities in this field. Many health companies engage in education programs and capacity building which are essential to develop heath worker skills in many countries, especially LMICs. We recommend that the IACG recommendations include the private sector, and in particular the role of the healthcare industry, as a valuable resource.	M
	b) Ethical production, distribution and marketing practices, including through environmentally sustainable production and waste management and the elimination of inappropriate incentives to sell antimicrobials;	This bullet point is confusing as it seems to conflate promotional activities with manufacturing. If a manufacturing bullet is desired, we would	Н



		suggest that it aligns to the principles set forward by the AMR Alliance ¹ , encouraging all manufacturers to align policies to those defined by the AMR Alliance manufacturing framework.	
	c) Engagement by the private sector in collaborative efforts to collect, analyze and use data and realign economic incentives to improve production, distribution and marketing practices;	There does not seem to be any detail about the marketing practices anywhere. The inappropriate incentive point above is the key one – would suggest deleting "marketing".	M
p. 11 (page 12), bullet point no. 1 on "Considerations for this recommendation (C2)"	"The IACG recognizes the diverse spectrum of private sector actors that need to be engaged in the fight against antimicrobial resistance, including pharmaceutical, health technology and pesticide/biocide industries, food producers and retailers, and banking, insurance and finance institutions."	This part is missing the importance of venture capital. It is also our proposal that the list include all of the healthcare industry sectors, including in vitro diagnostic industry.	M

¹ https://www.amrindustryalliance.org/shared-goals/common-antibiotic-manufacturing-framework/



p. 11 (page 12), bullet point no. 2 on "Considerations for this recommendation (C2)"	" collaborative approaches to prudent distribution and use of antibiotics , and through organized industry collaboration related to both human and animal health."	Suggest changing from <u>"antibiotics" to "antimicrobials"</u> , as this also includes vaccines (e.g. Gavi).	M
p. 11 (page 12), bullet point no. 3 on "Considerations for this recommendation (C2)"	"In addition to the activities described in the recommendation, private sector actors in human, plant, and animal health, as well as in the food production and retail sectors, have important contributions to make in the areas of financing and resource mobilization; information and data sharing; monitoring and surveillance; behaviour change and communication; advocacy and work with government on key policy issues; research and development, and effective environmental management."	There are many other sources of environmental discharge that are combined significantly higher than from manufacturing. e.g. agriculture, human waste, and hospitals, and other health care providers have significant more impact on environmental discharge of antibiotics. These major other sources should be noted in these sections.	Н
p. 12 (page 13), "Invest for a sustainable response" section D	[Aim of the recommendations in this section] "The recommendations further underline that domestic financing commitments by national governments are essential to advance priority actions and ensure longterm, sustainable responses to antimicrobial resistance."	On the contrary, the below recommendations that follow seem to concentrate on bi-/multi-lateral financing support. It should be noted that domestic governments must prioritise health policy and financing initiatives in this space and will play a leading role in the introduction of incentives.	Н



p. 12 (page 13), bullet point no. 1 on "Considerations for this recommendation (D1)"	"These costs may be offset by adequate investments to lower the burden of infections through water and sanitation, hygiene, vaccination and infection prevention and control measures."	We suggest adding "improving health systems" and "surveillance".	Н
p. 13 (page 14), bullet point no. 3 on "Considerations for this recommendation (D2)"	"The IACG highlights the importance of increased engagement by the private sector and other stakeholders to advance innovative financing concepts for antimicrobial resistance, including livestock insurance programs for transitioning of animal husbandry practices, accredited drug dispensing outlets and social impact bonds."	This bullet should reflect the extensive involvement of the private sector in advancing new models of collaboration through the public-private entities mentioned elsewhere in the Recommendations.	М
p. 14 (page 15), Recommendation E1 box	"The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat"	We welcome the implementation of a global governance to structure actions, measure progress and remove blocking points. We strongly recommend that the IACG recommendation paper emphasize the importance of having all of the sub-parts of the private sector included in such governance, as AMR is an important issue that requires a multi-sectoral approach. In addition, we recommend expanding the work of the One Health Global Leadership Group on Antimicrobial Resistance to education and increasing general public awareness.	Н



	c) Monitor and report on progress, gaps and accountability in the global response to antimicrobial resistance;	We suggest adding "Development and updating of National Action Plans".	М
p. 15 (page 16), bullet point no. 3 on "Considerations for this recommendation (E1)"	"The IACG proposes that the One Health Global Leadership Group for Antimicrobial Resistance be composed of a small group of current and former Heads of State, Ministers of Agriculture, Health and Environment, Heads of the Tripartite agencies, other UN and international agencies, Heads of Regional Banks and other prominent global leaders and eminent persons representing human, animal and plant health, as well as food production and the environment."	Given that a sustainable solution to AMR will require a coordinated response from <i>all</i> stakeholders, the private sector should also be represented on the One Health Global Leadership Group.	Н
p. 16 (page 17), bullet point no. 3 on "Considerations for this recommendation (E2)"	"The IACG notes that the composition of the Independent Panel should include representation across the One Health spectrum, including experts from human, terrestrial and aquatic animal and plant health as well as the environment, food production and food safety sectors."	We strongly support this view - a technocratic approach is not the answer. As this report itself champions, private sector must be engaged more.	Н
p. 16 (page 17), Recommendation E3 box	e) Guide, support, monitor and evaluate implementation, including on infection prevention, integrated surveillance, data quality and harmonization, risk assessment, and demand forecasting and supply management.	We suggest including innovative business models and procurement systems.	М

Aviva

Aviva input on draft recommendations of the ad-hoc Interagency Coordination Group on AMR.

As a global insurer and asset manager, we are always doing what we can to be at the forefront of responsible investment, identifying emerging issues that are likely to impact on companies' performance and the society in which they operate. When we identify an issue, we will work to understand how companies and society are impacted and engage with them either individually or collaboratively to deliver change. We believe that the issues related to antimicrobial resistance pose serious risks to the public health and business landscape. Aviva Investors meets individually and collectively with the companies it invests in, predominantly in the pharmaceutical, food retailer and producer sectors to discuss their strategy on antibiotic resistance. We encourage our investee companies to establish a comprehensive antibiotics policy that includes clear timelines for phasing out routine, prophylactic use of antibiotics across all livestock, seafood and poultry supply chains. Following extensive engagement several companies have committed to phasing out antibiotic use (see appendix for more background on our work on AMR).

We welcome the opportunity to comment on the draft recommendations of the Interagency Coordination Group (IACG) on antimicrobial resistance. The recommendations rightly highlight the prevalence of AMR throughout a range of industries and the responsibilities of a broad range of companies: from pharmaceutical to producers and food retailers. As a result, we would like to highlight the crucial role that investors can have in ensuring these companies take into consideration the risk of AMR. We believe the recommendations in the current draft do not adequately mention and articulate the role of private financial institutions and encourage the IACG to mention the role of private capital markets in the recommendations and integrate AMR as part of the discussions taking place at the United Nations on sustainable finance.

Indeed, the United Nations Secretary General's Strategy for Financing the Agenda for Sustainable Development (2018-2021) highlights the importance of aligning financial systems with the 2030 Agenda and the need to have policies and regulations that encourage the rising demand for, and supply of finance for sustainable activities. It also mentions that "private financial institutions have also been working with the UN to understand today's environmental, social and governance challenges and why they matter to finance" and we want to encourage the IACG and future global work on AMR to be part of these discussions to make the capital markets more sustainable. As a result, we would urge that recommendations don't consider private actors only as donors, as it does in the current phrasing "public, private and philanthropic donors", but articulates more clearly in each of these recommendations (B and D2) a mention of private finance as a source of funding to contribute to addressing antimicrobial resistance.

We support recommendation C2 since it highlights the role of the private sector as a key stakeholder. We would encourage the integration of a new section under the considerations for this recommendation focused on the role of investors. Private investors can have significant leverage on how companies behave (see appendix one for example of our engagement with companies) and we believe it is worth noting that investors should be encouraged to engage with companies to mitigate the AMR risk and drive improvements within the food, farm and pharmaceutical sectors.

We support the reference to the need to elevate the challenges of antimicrobial resistance as crucial elements of the financing agenda, including the SDGs, and the urgency to develop robust indicators that capture the direct and indirect impact of AMR on efforts to achieve the SDGs. We encourage the IACG to mention the role that benchmarks can have – such as the Antibiotic Resistance Benchmark and consider ways in which these could be used to direct financing and investments towards companies that are best performers.

Aviva: Internal

We would recommend adding a direct reference to sustainable finance in the draft recommendations under section D "Invest for a sustainable response" with a clear mention of private finance. We would encourage the inclusion under D2 that "the IACG emphasizes the need for increased investment in the global response to antimicrobial resistance, from public and private financing."

We look forward to further contributing to the work of the IACG and seeing the final recommendations that will be submitted to the UN Secretary-General. Considering the activities taking place at UN-level on financing for development on how to align private finance with the Sustainable Development Goals, we encourage you to raise the issue of AMR financing and how private financial actors should consider it with the same level of engagement that exists on climate financing.

Appendix one: Background to Aviva's work on anti-microbial resistance

Aviva Investors convened and chaired the first ever investor conference on antibiotic resistance with the UK Government's Antimicrobial Resistance Review team, with Lord Jim O'Neill as our keynote speaker.

We are proud to be a founding signatory to the Farm Animal Investment Risk & Return (FAIRR) investor initiative which has brought together a coalition of more than 70 institutional investors managing over \$2.5 trillion. The coalition is calling for an end to the routine, non-therapeutic use of antibiotics in companies' supply chains.

In World Antibiotics Awareness Week we launched <u>Superbugs and Super risks: A Guide for</u> Investors in collaboration with FAIRR.

We have engaged collectively and individually with the companies we invest in, mainly in the pharma, food retailer and producer sectors to discuss their strategy on antibiotic resistance. The most noteworthy outcome to date came with the announcement that McDonald's would remove antibiotics that are critically important for human medicine from their global broiler chicken supply chain. Our former CEO Mark Wilson wrote to the CEO of McDonald's to congratulate him on the significance of this milestone for McDonald's and for the industry.

We also made AMR a central tenant of both our flagship client conferences in 2017.

In 2017, we were the only insurer and investor to be invited to address the Call to Action Conference on Antimicrobial Resistance, convened by Dame Sally Davies, the UK's Chief Medical Officer, the UN Foundation and UK Government and at the invitation of the Wellcome Trust.

At the July 2018 EAT Forum our former CEO Mark Wilson gave a keynote on sustainable agriculture and launched our latest report that covers AMR. You can read our full report on sustainable agriculture <u>here</u>.

In September 2018 we co-convened Super Bugs and Super Risks: The Role of the Private Sector with the EBRD. Dame Sally Davies, England's Chief Medical Officer was the key note speaker at the conference. It was followed by roundtable discussions by representatives of the private sector, public entities, civil society, international AMR experts and patients. One of the recommendations made by Aviva was the creation of a task force similar to the Task Force on Climate-related Financial Disclosures but focused on AMR to highlight the economic and prudential risks that AMR poses.

Aviva: Internal

Centrient Pharmaceuticals

Centrient Pharmaceuticals Input to IACG Draft

On behalf of Centrient Pharmaceuticals, we welcome the progress of the IACG in their important work on AMR and are pleased the private sector is recommended for inclusion as a key One Health stakeholder. Please find below our feedback on the draft recommendations for your consideration.

Recommendation:

Major procurers of antibiotics such as governments and others can use their buying power to effect change on the supply chain by sourcing only sustainably-produced ("clean") antibiotics. The IACG should include a policy recommendation on sustainability criteria in public procurement as a tool to ensure responsible, pollution-free manufacturing which does not contribute to AMR (similar to that proposed in new UK National Action Plan).

Justification:

Environmental pollution from antibiotic manufacturing is a contributor to AMR yet is only once explicitly mentioned in the Recommendations (C2) and only in the context of industry responsibility. While industry has made progress via the AMR Industry Alliance in establishing a framework and limits on antibiotic discharge, still yet the majority of antibiotic manufacturers (particularly in India and China) have not committed to these standards. From a governmental perspective, in India, legislation attempting to establish discharge targets nationally for manufacturers is in progress but delayed. Thus with no enforceable minimum standards in place, global procurers of antibiotics continue to source drugs made from factories which through their production processes may be contributing to AMR. The passage in the recently released 2019-2024 UK National Action Plan forms a good basis for a potential solution to the problem of irresponsible production through sustainable procurement.

Link to draft Recommendations:

The draft IACG Recommendations make mention of procurement and sustainable production (below) yet do not explicitly link these two themes together:

- Recommendation A1: Reference to "pooled procurement" and "developing national instruments based on international standards"
- Recommendation A2 : Reference to "Strengthening ... procurement of health commodities and waste management"
- Recommendation C2: Reference to "Ethical production, distribution and marketing practices, including through environmentally sustainable production and waste management and the elimination of inappropriate incentives to sell antimicrobials"

Encouraging the sustainable production of antibiotics through the power of procurement could be prove an effective tool in ensuring responsibility and accountability throughout the supply chain.

Reference Example:

On January 24th, the UK government released their new <u>National AMR Action Plan for 2019-2024</u> and among the key commitments, the plan proposes the use of procurement and certification as tools to ensure sustainably produced antibiotics are sourced (pages 47-48). The UK commits to:

- Work with other countries to ensure responsible antimicrobial procurement from manufacturers with transparent world class environmental stewardship in their supply chains
- Collaborate with industry to promote the development of a global environmental stewardship certification system that can distinguish responsible manufacturers of antimicrobials.

By including a comparable mention, the IACG could support countries to similarly adopt such National Action Plan policies and strengthen the impact of using sustainable procurement as a means to fight AMR.



Statement for submission to IACG recommendations on AMR

Investors recognise the routine non-therapeutic use of antibiotics in livestock production as a leading cause of rising antimicrobial resistance, and therefore a major risk to public health.

Antibiotic resistance is a material risk not only for food companies but presents a systemic risk across multiple sectors including the pharmaceutical, healthcare and insurance industries.

Immediate action is required to preserve the efficacy of antibiotics against diseases in both humans and animals. Investors view reform of the non-therapeutic use of antibiotics in livestock production as both necessary to protect public health and as essential to risk mitigation and long-term value creation, and therefore material to evaluating a company's prospects and to investor portfolios.

One of the most effective mechanisms for institutional investors to drive the judicious use of antibiotics in food supply chains is active ownership and stewardship through company engagement and voting. Aviva works individually and in collaboration with investor platforms such as the FAIRR Initiative to drive antibiotics stewardship in food production using a list of targeted questions for companies and <u>best practice policy</u> on antibiotics stewardship that was developed in in consultation with leading industry and issue experts to provide guidance to food companies. Aviva is also a signatory to the Global Investor Statement on Antibiotics, coordinated by FAIRR.

Engagement questions for food companies

- 1. Does the company have an antibiotics policy publicly available on its website?
- 2. What is the scope of the policy?
 - o Does it cover animal-derived proteins sources across all its operations and across all relevant species?
 - o Does it cover all antibiotics, or it is limited to a certain class of antibiotics only (for example, critically important antibiotics)?
- 3. How strong is the commitment? For example:
 - Does it only prohibit growth promotion?
 - Does it prohibit all routine uses of antibiotics i.e. growth promotion and prophylactic use?
- 4. Does the policy commit to specific targets and timelines for all species?
- 5. Does the company commit to third-party auditing and monitoring?
- 6. Does the company report on progress, including levels of antibiotics use?

HealthforAnimals

Hospitals and Healthcare Settings (Recommendations A1 & B3)

The recommendations discuss animal and food production, yet, do not address hospital, clinics, or other healthcare facilities. This is a <u>major omission</u> considering the European Centre for Disease Prevention and Control states <u>"75% of disease linked to resistant bacteria is due to healthcare-associated infections."</u> Simple steps in human healthcare settings such as handwashing could reduce these infections significantly, according to the OECD's recent report – <u>'Stemming the Superbug Tide.'</u>

Therefore, we strongly recommend the IACG add clear, actionable steps for policymakers to address AMR transfer in hospitals, clinics or other healthcare facilities. This could be done by:

- 1. In Recommendation A1, adding a new bullet in the A-F list which states: "Reducing the transfer of bacteria in healthcare facilities through strict protocols on handwashing and hygiene along with other best practices."
- 2. In Recommendation A1, Considerations for This Recommendation, adding a bullet which states: "The IACG recognizes that, according to the European Centre for Disease Prevention and Control, 75% of disease linked to resistant bacteria is due to healthcare-associated infections. Therefore, putting in place best practices to limit transfer of bacteria within these settings is essential. Strict handwashing and hygiene protocols can be rapidly implemented by all facilities to make an immediate impact on AMR transfer."
- 3. In Recommendation B3, adding a new bullet in the A-D list which states: "Promoting the rapid uptake of strict handwashing, hyenine and other best practice protocols that can reduce resistant bacteria transfer in healthcare settings".
- 4. In Recommendation B3, Considerations for this Recommendation, adding a bullet which states: "The IACG notes that research shows most resistant bacteria transfer in people occurs in healthcare settings such as hospitals or clinics. Promoting these results to nations where strict hygiene protocols are not the norm can have an immediate impact on AMR."

Regulatory Environment (Recommendation A1)

On Page 4, under the Recommendation A1, Considerations for this Recommendation, the IACG lists numerous ways we can better ensure access and stewardship of medicines. This is a laudable goal. One area that is not listed and should be included is improving the regulatory environment for new medicines and vaccines. This is a significant hurdle, especially in smaller or less developed markets. Therefore, we recommend the IACG include the following bullet:

1. Improving the regulatory environment for new medicines and vaccines: Governments should consider the regulatory requirements for the review and market authorization or license of new medicines and vaccines. Governments would benefit from removing unnecessary or redundant mechanisms in evaluating the safety or efficacy of a candidate medicine or vaccine. Some Member States also use certain medicine or vaccine review processes as a non-tariff trade barrier to protect domestic production. However, these barriers limit access to medicines, veterinary products, or vaccines that could reduce the need for a medically important antimicrobial.

Growth Promotion (Recommendation A3)

The wording of Recommendation A3 is unclear. It could be interpreted as two recommendations – a 'phase out of the use of antimicrobials for growth promotion' AND an 'immediate end to the use of the Highest Priority Critically Important Antibiotic Agents.'

At the Private Sector Briefing, the IACG made clear that the recommendations *only* called for an end to the use of the Highest Priority Critically Important Antibiotic Agents for growth promotion purposes. In addition, the recommendation states it is consistent with the guidance from the tripartite agencies. This is not fully accurate.

- The WHO AMR Global plan, and the Tripartite's <u>Global Framework for Development & Stewardship to Combat Antimicrobial Resistance</u> states "*Phase out the use of antibiotics for animal growth promotion and plant protection in the absence of risk analysis.*"
- The OIE <u>states that</u> "responsible and prudent use of antimicrobial agents does not include the use of antimicrobial agents for growth promotion in the absence of risk analysis."
- The FAO states in their <u>2016-2020 Action Plan on AMR</u>: "prevent the unnecessary use of antimicrobials, including the phasing out of antimicrobials as growth promoters (veterinary antimicrobial drugs which belong to or are able to cause cross resistance to classes of antimicrobial agents used or submitted for approval in humans and animals in the absence of a risk analysis)."

All Tripartite members call for phasing out of growth promotion 'in the absence of a risk analysis.' The IACG does not include this phrase, therefore, the guidance is not consistent with the Tripartite.

We recommend the IACG change the text to read: *The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion in the absence of a risk analysis, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the growth promotion use of the Highest Priority Critically Important Antibiotics Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides, and ketolides, glycopeptites and polymixins).*

This change would make the text clearer and in line with the recommendation of the Tripartite agencies.

Animal Health R&D Challenges (Recommendation B1)

Recommendation B1 calls on the private sector to increase investment and innovation in new antimicrobials. We acknowledge this request, but, ask the IACG to consider the unique investment challenge that exists in animal antibiotic development. If an animal health company discovers a new antibiotic, then determines it is also efficacious in humans, most major markets will reserve this antibiotic for human use only. This severely limits the innovation opportunities for animal health companies which may only bring to market an antibiotic which cannot be authorized for use in humans.

Therefore, we recommend the IACG include the following:

2. Add a bullet In Recommendation B1, Considerations for this Recommendation that states: The IACG acknowledges that development of antimicrobials in animal health is uniquely difficult. New antimicrobials that are also efficacious in people will be reserved for human use in major markets. This puts significant limits on research opportunities and possibilities for new antimicrobial discoveries in animal health.

This will add balance and nuance to this recommendation to better inform member states.

Additional consideration to include under Recommendation A1

In the Considerations, a major point related to the use of antibiotics in animal health is missing. We suggest the text below is inserted as the second or third last bullet: "Driving reasons for the use of antibiotics in animal health - especially in many low- and medium-income countries - are the large and growing animal disease challenges, the fast-growing scale of animal production, and structural underinvestment in animal health. These underlying issues must be addressed as part of the drive to diminish unnecessary use".

Animal Health Research Funding (Recommendation D2)

We appreciate Recommendation D2 including a call for increased investment in the global response to AMR. However, the list (Gavi – The Vaccine Alliance, The World Bank, the Global Fund to Fight AIDS, etc....) are primarily human health financing mechanisms.

At the moment, there are no animal health financing mechanisms at a similar level to these organizations. Therefore, we recommend the IACG make two changes:

- 1. Change the Recommendation text to: The IACG emphasizes the need for increased investment in the global response to antimicrobial resistance. It urges existing and future financing mechanisms in human, animal and plant health, as well as food production and the environment including Gavi the Vaccine Alliance, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Global Financing Facility, Multilateral Climate Funds, Unitaid, as well as future financing streams for Universal Health Coverage and other priority development issues, and their donors to give antimicrobial resistance greater priority in their resource allocations, and recognizes the significant gap in research funding and financing mechanisms available to animal health compared to human health. It further calls upon public, private and philanthropic donors in human, animal and plant health, as well as food production and the environment, to increase funding to contribute to addressing antimicrobial resistance, including to support implementation of National Antimicrobial Resistance Action Plans.
- 2. Add a bullet under' Considerations for this Recommendation' which states: the IACG acknowledges that animal health research receives far less financing than human health. This limits the funds available to develop tools that can address AMR in animals and reduce the need for antimicrobials. Increased public funding or development of financing mechanisms for animal health is essential to addressing AMR.

This would help spur development of financing mechanisms and increases in animal health research funding that can help address AMR.

Global Leadership Groups Clarifications (Recommendation E1 and E2)

The IACG has provided a clear and significant call to action within Recommendation E1 and E2. Creation of this 'Global Leadership Group on Antimicrobial Resistance' and the accompanying 'Independent Panel on Evidence for Action against Antimicrobial Resistance' could be valuable, however, much more detail is required for evaluation.

As a result, we do not have specific text edits to suggest. The requisite detail is missing. Therefore, we urge the IACG to consider and address the following questions within Recommendations E1 and E2:

- 1. Who will drive the development of the Global Leadership Group? The IACG's mandate will expire at the September UN General Assembly. Therefore, it is unclear who the IACG wants to take up the mantle and drive this action forward. This is necessary to ensure ownership and action.
- 2. Will the 'Global Leadership Group' be a UN, Tripartite or independent body? It is not clear who the Global Leadership Group will report to. For example, it could be a new UN (sub) body, a function of the tripartite or something else.
- **3.** What will be the mechanism for democratic control and oversight? The WHO, FAO and OIE are member driven organizations and each has an assembly of member countries which exert democratic oversight over its activities. How will exert oversight and democratic control; over the activities of the Global Leadership Group?
- 4. Will the Global Leadership Group work in parallel to the Tripartite or coordinate and direct the Tripartite? It is not clear within the proposal whether the Global Leadership Group will have different responsibilities and actions from the Tripartite, or, whether it will be a new entity to direct and coordinate the Tripartite agencies. This clarity is needed to understand how the Global Leadership Group would fit into the existing structures.
- **5.** How will the Global Leadership Group measure success? The current proposal needs more clarity on the objectives of the Global Leadership Group and the 'key performance indicators.' The items outlined in Recommendation E1, A-H are extremely broad. More specificity is required to evaluate whether the Global Leadership Group's goals are achievable.
- 6. How will the Global Leadership Group succeed where the Tripartite has not? The IACG states that Tripartite efforts must be 'stepped up.' It's not clear within the recommendations or considerations how the Global Leadership Group will succeed, in areas where the IACG believes the Tripartite is lagging, and how the Global Leadership Group would address the practical on the ground help that most (LMIC) are asking input on?

Recommendations E1 and E2 are interesting and could be valuable. However, much more detail is required to support this activity and understand how it comes to fruition.

International Meat Secretariat

From: <u>hsin.huang@meat-ims.org</u>

To: <u>IACG-secretariat</u>

Subject: Draft Recommendations of the Ad hoc IACG on AMR

Date: Tuesday, February 19, 2019 17:19:45

Dear IACG Secretariat,

The International Meat Secretariat thanks the IACG for these draft recommendations, which are a useful way forward.

We would like to make one comment on recommendation A3:

"The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins)."

We would suggest that this recommendation be aligned with WHO and OIE recommendations.

Sincerely, Hsin Huang

Secretary General International Meat Secretariat

International Poultry Council (IPC)

Regarding: DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE - January 2019 Draft

Comments for consideration submitted by:



International Poultry Council 2300 West Park Place Blvd., Suite 100 Stone Mountain, Georgia, USA 30087 www.internationalpoultrycouncil.org By: Marilia Rangel R. M. Campos Secretary General

February 26, 2019

The International Poultry Council (IPC) commends the collaborative efforts of IACG to address antimicrobial resistance and provides the following comments for consideration regarding the January 2019 "Draft Recommendations of the Ad Hoc Interagency Coordination Group on Antimicrobial Resistance".

Currently, IPC has 23 Country Members and 52 Associate Members. IPC Country Members represent more than 95% of the global poultry trade and more than 90% of poultry production. IPC and its members advocate for the responsible use and stewardship of all antimicrobials, the need to protect the health and welfare of our birds, to produce safe food, to safeguard the efficacy of antimicrobials, and to build trust with consumers. IPC and its members are actively engaged with intergovernmental organizations, governments and stakeholders to help shape public policy to address antimicrobial resistance. We are active in advancing the 'One Health' approach leading to healthy people, healthy animals and a healthy planet.

Specific to the IACG draft the following comments are for your consideration in drafting the final report:

Recommendation A1 and A2: Important to fix priorities at the national level and that they also consider internationally agreed standards, guidelines and information developed by the Tripartite.

Recommendation A3: IPC supports that those antimicrobials critically important for human medicine should be used for therapeutic purposes only (disease treatment, disease control and disease prevention) and under a supervising veterinarian's diagnosis and oversight whether in feed, water or via injection. Further those antimicrobials not important for human medicine can be approved for therapeutic uses (disease treatment, disease control and disease prevention), and based upon a risk assessment, for other uses, and can be used in feed, water or via injection. Importantly, countries need a regulatory structure for all antimicrobials with stringent regulatory controls based upon sound science-based risk analysis principles and sound stewardship principles and practices in order to support minimizing antimicrobial resistance development and transfer.

Recommendation B1 and B2 and B3: Generally, support these recognizing there is a critical role for both governmental and private sector stakeholders.

Recommendation C1 and C2: Consider profiling higher role for producer organizations such as IPC that can leverage their membership base to engage, shape and share use policies and practices.

Recommendation D1 and D2: Consider leveraging and further investing in existing international and governmental organizations and industry structures. It is critical to maintain science-based and commonly agreed upon international standards and guidelines.

Recommendation E1 and E2: Rather than create a new structure and a new scientific group, suggest leveraging existing structures and working through current Tripartite governmental organizations. And then more actively leverage engagement of producer organizations and private sector to incorporate best practices into ongoing business practices. IPC believes that the successful progress in addressing antimicrobial resistance through the Tripartite demonstrates that they are up to the task and that it would be a diversion of focus to establish a new structure and scientific group.

Recommendation E3: Support as drafted where focus is to leverage existing structure, roles and organizations.

IPC is pleased to provide our comments for consideration and inclusion in refining the existing draft. IPC recognizes the ethical obligation of farmers and their veterinarians to protect the health and welfare of the birds in their care, which may include the responsible use of antimicrobials. Yet, IPC accepts that the poultry sector needs to adopt management practices, and provide education regarding such practices, that reduce the use of those antimicrobials for which resistance could pose the greatest global risk. IPC is pleased to be an active stakeholder in addressing antimicrobial resistance as part of a 'One Health' effort.

International Union of Food, Agricultural, Hotel, Restaurant, Catering, Tobacco and Allied Workers' Associations (IUF)

From: <u>James Ritchie IUF-UITA-IUL</u>

To: <u>IACG-secretariat</u>
Cc: <u>Svetlana Boincean</u>

Subject: Draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance

Date: Tuesday, January 29, 2019 15:05:31

Attachments:

Dear IACG Secretariat members,

The IUF wishes to make the following submission on the draft recommendations of the Ad hoc interagency coordination group on antimicrobial resistance.(AMR)

The International Union of Food, Agricultural, Hotel, Restaurant, Catering, Tobacco and Allied Workers' Associations (IUF) is an international federation of trade unions representing workers employed in agriculture and plantations; the preparation and manufacture of food and beverages; hotels, restaurants and catering services; all stages of tobacco processing. The IUF is composed of 421 affiliated trade unions in 128 countries representing over 10 million workers.

The hazards posed to workers in intensive livestock raising and in slaughtering, processing and food preparation by AMR pathogens have not been adequately recognized by the international agencies working on AMR.

The IUF has approached the International Labour Organization (ILO) to request it become more actively involved in the interagency work in order that the workplace risks can be adequately identified monitored and reduced, with a long term goal of elimination of the hazard.

Worker health and safety has been almost completely ignored in the global fight to contain AMR. Antimicrobial resistance is a work-related hazard. Advising behavior modification is not an adequate response to the workplace hazard. The workplace contaminates the worker, it is not the worker which contaminates the workplace.

The infection of a worker by AMR pathogens must be internationally recognized as a work related disease in occupations where workers are exposed to the hazard. There should be regular health screening of workers exposed to the hazard and notification to regulatory agencies should be compulsory when AMR pathogens are discovered in processing plants or on farms.

National Governments should ensure that workers are covered for any medical expenses for screening and any treatment and that any time off work which arises from the contraction of an AMR pathogen should be paid time.

Employers in conjunction with health authorities should provide training on ways in which workers can protect themselves.

Hospital workers and other health providers are outside our jurisdiction but these workers have been exposed to AMR pathogens for several decades.

I attach a resource on AMR as a workplace hazard that the IUF prepared for its affiliates.

Please do not hesitate to contact me if you have any queries or require any clarification.

Yours sincerely

James

James Ritchie Assistant General Secretary IUF-IUL-UITA

RPS Diagnostics, Inc.



RPS Diagnostics, Inc. 7227 Delainey Court Sarasota, FL 34240

February 19, 2019

UN-Secretary General Interagency Coordination Group (IACG) on Antimicrobial Resistance

Re: Public discussion - Draft Recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance

Dear Secretary General,

I am writing in response to the call for public comment pertaining to the **Draft Recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance.** As a company focused on providing affordable point-of-care (POC) tests that diagnose a host immune response to infectious diseases and thus enable healthcare providers to accurately diagnose and provide appropriate and timely treatment that can lead to a reduction in antibiotic misuse, adverse events and healthcare costs, we support the efforts of the United Nations Member States that form the IACG and to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance.

Thank you for the opportunity to provide comment, upon review the draft recommendations I would like to submit the following feedback:

1. Member States should consider piloting a <u>'Test Before Treat'</u> policy that would require a positive point-of-care (POC) diagnostic test prior to prescribing antimicrobials to patients who would be more likely to experience harm than benefit such as in acute respiratory infections (ARI). Acute respiratory infections (ARIs) are contagious and represent one of the most common reasons patients seek medical attention worldwide. ARIs range from the common cold to pneumonia, Influenza, and Strep throat, among others. The overlap in clinical presentation poses a

challenge for clinicians to identify a clinically significant infection as well as differentiate viral from bacterial infection in the outpatient setting. Diagnostic uncertainty combined with patient pressures influence physicians to prescribe antibiotics for more than 50% of ARIs, despite frequent nonbacterial etiologies in which antibiotics are ineffective (Harris, Hicks et al. 2016). Rapid, POC diagnostic tests that have proven to be safe, easy-to-use, accurate and affordable, should be leveraged to avoid unnecessary antibiotic prescription (or over the counter purchase) that drives resistance. Furthermore, it is important that the POC diagnostics are adept at identifying the host immune response to a bacterial or viral infection be deployed in the 'Test before Treat' initiative. Often times, highly sensitive molecular testing modalities can identify a trace amount of a pathogen that may colonize the area tested (e.g. the throat) or may be resolving from a previous infection (i.e. convalescent phase of an infection). For this reason, highly sensitive molecular pathogen identification testing may in fact lead to more antimicrobial prescriptions

A study by the Foundation of Innovative Diagnostic tests determined that the lack of POC testing costs a developed nation such as the UK with 65M people, approximately US \$250M annually [Submitted to BMC Health Research 12-2018] and leads to more than 50% overtreatment of viral conditions with unnecessary antibiotics. The cost savings and reduction in antibiotics is directly correlative to population size.

Therefore, it is important to consider rapid, POC diagnostic tests that utilize host immune response biomarkers to distinguish pathogen presence (colonization/carriage) from a clinically significant infection that warrants treatment in order to reduce antibiotic misuse. The 'Test Before Treat' pilot program should evaluate the usability of the POC diagnostic as well as the impact on antimicrobial prescriptions, related adverse events as well as associated healthcare costs to assess impact at the patient, healthcare system, and country level.

- 2. Recommendation B1: The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials for human, terrestrial and aquatic animal and plant health through:
 - a. RPS Comment: Although public, private, and philanthropic funding is essential to develop new antibiotics, diagnostics, vaccines and as well as safe alternatives to antimicrobials, in parallel, Member States should also work with their local governmental agencies to develop safe, expedited regulatory approval pathways and reimbursement strategies for *low risk and cost effective* POC diagnostic devices that show highly accurate performance data. In these instances, Member States should

consider conditional approvals that enable market access while safety, efficacy, and cost effectiveness data are collected. Without subsidizing (reimbursing) the general practitioners or urgent care providers to adopt low cost POC diagnostic testing, there is no practical way to incentivize behavior change and adoption of cost-effective strategies. If the practitioners perceive any loss or risk to their personal income due to lack of reimbursement, even though testing may dramatically limit the overuse of unnecessary antibiotics and resultant microbial resistance at a societal level, any benefit from the POC test will not be realized.

- 3. Recommendation E2: The IACG requests the Secretary-General, in close collaboration with the Tripartite agencies (FAO, OIE and WHO), UNEP and other international organizations, to convene an Independent Panel on Evidence for Action against Antimicrobial Resistance in a One Health context to monitor and provide Member States with regular reports on the science and evidence related to antimicrobial resistance, its impacts and future risks, and recommend options for adaptation and mitigation.
 - **a.** RPS Comment: The Independent Panel on Evidence for Action against Antimicrobial Resistance reports should also be inclusive of strategies for mitigating risk for developing antimicrobial resistance. Specifically, the reports should include the availability and utilization of rapid, accurate, POC diagnostics that can reduce antibiotic misuse, resistance, and cost.

Thank you for your consideration.

Sincerely,

Rob Sambursky, MD President & CEO

RPS Diagnostics

RPSdetectors.com

FebriDx.com

From: Heikinheimo, Annamari
To: IACG-secretariat
Subject: AMR public discussion

Date: Tuesday, February 19, 2019 22:59:39

To whom it may concern,

Thank you for the work of IACG for its's work to prevent the development and spread of antimicrobial resistance, which is one of major global health threats at the moment.

The IACG's list of different actions are important and essential steps towards the goal:

- A) Accelerate progress in countries;
- B) Innovate to secure the future;
- C) Collaborate for more effective action;
- D) Invest for a sustainable response; and
- E) Strengthen global accountability and governance.

However, as a university teacher and researcher, I would like to bring up and highlight some of the urgent educative needs in specialist training in all member states:

- At the moment, the environmental bacteria has been identified as a major reservoir for many AMR gene. However, some of the AMR genes are naturally present in the nature and some of them are acquired and enriched by the massive amount of antimicrobilas released to the nature. In the future, the research has to be addressed to be able to differentiate the natural resistance in the environment from the acquired resistance.
- One of the urgent priorities is to avoid the release on antimicrobials to the nature. Especially the pharmaceutical industry should be engaged to this. All Member states should work together towards this goal.
- One Health approach is important in education of the specialists. In Finland, veterinarians already study one year (their sixth study year) food safety and environmental hygiene. This includes all above mentioned aspects of AMR development and spread, including prudent use of antimicrobials and infection prevention with hygiene etc. I highly encourage that this teaching could be exported to other countries as well.

Yours sincerely, Annamari Heikinheimo

(I am representing a university teacher, researcher and a veterinarian, and here is my affiliation):

Annamari Heikinheimo, DVM, PhD
University lecturer
Dept. of Food Hygiene and Environmental Health
Faculty of Veterinary Medicine
University of Helsinki
Finland

Babacar Ndoye

Recommandations AMR

Dear colleagues,

I work as an expert consultant supporting countries in the development and implementation of national AMR plans, and as you know, sub-Saharan African countries are far behind the rest of the world in this area.

There may be many reasons, but the lack of support from policymakers and decision makers is one, and it is certain that the acquisition of this important support to technicians would accelerate the progress made in these countries.

The suggestion of recommendation that I would like to make, in the framework of recommendation A, is to put a particular emphasis on an important stakeholder that is the National Assembly that is supposed to represent the people and control the actions of the government.

A special letter of information and awareness raising could be formally addressed to all National Assemblies of Member States, without focusing on any region of the world, and I am confident of its positive effect on accelerating progress on the fight against AMR.

Prof. Babacar NDOYE

AMR/IPC Expert- consultant

Senegal

Daniel Carucci, Global Medical Director, McCann Health

From: <u>Carucci, Dan (NYC-MHNY)</u>

To: <u>IACG-secretariat</u>
Cc: <u>Kate Dodson</u>

Subject: Draft IACG feedback - need to reduce demand for antibiotics

Date: Monday, February 18, 2019 23:34:56

From:

Daniel Carucci, MD, MSc, PhD Global Medical Director McCann Health New York, NY

To the IACG Secretariat,

The antimicrobial resistance we see today is not a natural phenomenon; humans are responsible for this crisis through their widespread use, misuse, and misunderstanding of antibiotics. Efforts to curb over-prescription of antibiotics in the medical setting or to reduce reliance and use in the veterinary setting have not been sufficiently balanced by efforts to increase awareness of antimicrobial resistance and reduce demand of unnecessary antibiotic use by patients and consumers. Patients often expect physicians to prescribe antibiotics for common viral illnesses; and physician are persuaded to do so. Agricultural use of antibiotics has become commonplace and consumers are generally unaware of the effect antibiotics consumed through food products can have on their health and that of their families. Antibiotics are also often unregulated, of dubious quality, and are too easily available in many of the most resource-poor areas of the world. Furthermore, both the general public and many health professionals are unaware of the growing body of evidence linking antibiotic consumption with alterations in the microbiome, its association with obesity, mental health, and other health conditions. Few truly understand the magnitude of the problem being created by a medical advancement so revered, and yet so often misunderstood. Beyond the traditional advocacy and communications directed toward professionals and emphasized by the draft IACG guidelines, renewed efforts are desperately needed to develop evidence-based public communications that address the demand-side of "One Health"; targeting patients, consumers, and the general public about what antibiotics should mean to them so that they can make informed and empowered decisions. The approach offered here goes beyond behavior change to the heart of creating empowered health consumers, who are a powerful force in societal change.

To ensure country and policy leaders are aware of the importance of a renewed focus on increasing awareness of the AMR risks and reducing the demand for antibiotics, the following is offered for consideration by the IACG secretariat:

Recommendation AI. d. Supporting behaviour change [including reducing provision of antibiotics by professionals, as well as reducing antibiotic demand by patients seeking care and consumers through their purchasing decisions] through [evidence-based] effective [public] communication and incentives targeted at the public and professionals in human, terrestrial and aquatic animal and plant health, as well as food production and the environment

Considerations for this recommendation

• [Existing recommendation] The prudent use of antimicrobials across the human, animal, plant and environmental health sectors requires appropriate attention to and investment in training, accreditation and regulation of professionals, including physicians, pharmacists,

- veterinarians and other specialists across human, terrestrial and aquatic animal and plant health, as well as in food production and the environment. The IACG recognizes that in settings where trained prescribers are in short supply, non-physicians (such as nurses, paramedics and community health workers) and veterinary paraprofessionals may also be trained and authorized to prescribe or administer some antimicrobial agents.
- [While communications and training efforts targeting professionals are urgently needed, large scale, evidence-based, public communications strategies and campaigns should also be developed and integrated into these efforts to increase awareness of AMR risks and reduce the demand for antibiotics by patients from their providers and by consumers in their purchasing decisions. The development of these regional and national campaigns should also leverage the experience and resources of both the public and private sectors.]

DANIEL CARUCCI, MD, MSC, PHD | GLOBAL MEDICAL DIRECTOR



Heidi Vesterinen, Researcher, One Health Workforce, University of Minnesota

From: Heidi Vesterinen

To: IACG-secretariat

Cc: <u>Saija Kalenius</u>; <u>Jeff Bender</u>

Subject: IACG draft recommendations on AMR Date: Monday, February 18, 2019 23:46:28

Dear readers,

Below is my personal feedback to the draft recommendations of the ad hoc interagency coordination group on antimicrobial resistance.

My main concern is that the document does not put enough emphasis on the importance of education. Education is mentioned briefly, and yet improving current education methods and designing and implementing new ones will be the key to achieving the outcomes described in the document.

More spesifically, I have he following comments on the document sections:

Recommendation A1

- Quality assured antimicrobial delivery requires building in country infrastructure for quality assurance, which is severely lacking in many places.
- Competent and licensed professionals need to be educated, and this workforce does not exist in many countries especially in animal and plant services.
- Ensuring equitable and affordable access, in addition to the six mentioned actions, requires heavy concentration on education (both vocational, academic and continuing). Even though training has been mentioned here, I feel it should get a much larger emphasis as it is such a core requirement.
- Supporting government-academia relationships in country would greatly help in developing the workforce suitable for each country.
- Tackling substandard and falsified products with low-cost track-and-trace systems could benefit from exploring block-chain protocols.
- Sound environmental and waste management practices aren not utilised routinely outside of large hospitals even in developed countries. This area needs major emphasis and multidisciplinary problem solving.

Recommendation A2

- In developing the national action plans, it would be vital to involve all stakeholders, including animal and plant health, as the Ministry of Health easily ends up leading this process.
- Countries will need support in taking the formed action plans to the field and implementing them.

Recommendation A3

- Again in here, in addition to legislation, education for farmers on effective use of antimicrobials is needed.
- Practical education for example in the form of facilitating farm visits to share best practices could support behaviour change.

Recommendation C2

- In many instances, traditional meeting formats and current reliability and access to virtual meeting modalities is not sufficient to produce systematic results within the available time when engaging multiple partners. This is why interdisciplinary and multistakeholder engagement can be seen as fruitless or frustrating.
- In order for systematic and meaningful engagement to be possible between the private sector, academia and the government within the resources available (such as time, funding and geography), new innovative tools for facilitating such engagement are needed.

Thank you for offering the change to comment. My comments are based on my expertise in animal & public health and the time I haves spent working in countries such as Finland, US, UK, India, Nepal.

Tackling AMR is one of the grand challenges of our time and IACG's hard work to form these recommendations is extremely important & valuable.

Sincerely,

Heidi Vesterinen, DVM, MPH, DACVPM,

Researcher | One Health Workforce University of Minnesota

Les Sims, Director, Asia Pacific Veterinary Information Services

From:
To: IACG-secretariat

Cc: Mark Schipp; Juan Lubroth (AGAH)

Subject: Comments on draft IACG recommendations on antimicrobial resistance (AMR)

Date: Tuesday, February 19, 2019 02:15:05

Attachments:

Thank you for the opportunity to review and comment on the draft recommendations.

I am commenting as an individual who has 20-plus years experience in global animal disease control and prevention with a strong One Health focus and a particular focus on East and South East Asia. My comments relate to the animal production side.

My main concern with the existing recommendation and approach is that they propose solutions that will work in high income countries but less well (or not at all) in low and low-middle income countries where levels of resistance are much higher and will prove to be more difficult to reverse.

Many of the lessons learned from the global response to H5 avian influenza from 2005 onwards are not being heeded. In particular, the limited reach of veterinary services and the relatively weak biosecurity in many production and marketing systems resulted in H5 viruses remaining endemic in a number of countries and sub-regions. These factors are changing slowly but will continue to constrain efforts to reduce levels of endemic diseases of production animals that result in AM treatments or to provide appropriate stewardship and supply of AMs by prescription.

A "One Health" approach is important and already well recognised. We now need to focus on what the animal production sector can do to reduce and limit the damage from AMR.

In fact, there is a limited range of tools available and some of these tools may not work as well as exepcted. Antimicrobial stewardship, while essential to prevent further deterioration in AMR, will likely only provide incremental benefits in terms of reductions in AMR in food animals, especially in low and low-middle income countries. The factors that get in the way of improving biosecurity in smaller scale farms (social and economic) are now well characterised but difficult to overcome despite best intentions and communications. Economic factors also affect choices on use of vaccines that might otherwise limit certain diseases.

The end result is that, 10 years from now in these countries, we will still have considerable resistance in food producing animals. Even in the countries implementing best practices for many years, such as Denmark, resistance to older AMs has persisted.

We need to get the balance right between monitoring, mitigation and adaptation. At present, there is too much focus on monitoring. Most countries have limited resources and it is easier to put these into monitoring programmes yet we know we have a problem with AMR in low and low-middle income countries from studies already undertaken. If we can only make limited gains in reducing AMR through mitigation measures we have to find methods to contain it (adaptation) so that resistance in food animals does not become a problem for humans and the environment. Adaptation is an area where we still do not have "off the shelf" measures that can be applied (unlike AM stewardship programmes used for mitigation).

I have enclosed a document that contains some alternative recommendations for the animal production sector for your consideration and would be willing to expand on any of these if required.

Yours sincerely

Les Sims Director Asia Pacific Veterinary Information Services

Alternative Recommendations for Food Animal Production Sector

Aspirational goals for 2030

1. For food animal production to make a very small contribution to AMR in humans and the environment

This will require both mitigation and adaptation because we may not be able to reverse much of the resistance that is already present, especially to older AMs (no fitness cost for resistance) in particular in low and low-middle income countries

2. For food animal producers to have access to appropriate AM treatments in the event of cases of disease caused by or associated with bacterial infections

This creates some problems in places where multidrug resistance is already present

Goals for all countries for the next 5 years

- 1. To prevent further increases in resistance in the food animal production sector and, where possible, to reduce levels of existing resistance (currently very high especially for older AMs and even some newer AMs) Mitigation
- 2. To reduce the risk posed by existing resistance genes in food animal bacteria through biocontainment given mitigation will not resolve the problem Adaptation

Ways need to be found to support low and low-middle income countries given these are generally the places with the highest levels of AMR bacteria

Mitigation.

I see six key concerns:

- i) Factors at farm level that have resulted in excess use of AMs (and high levels of resistance) will not change rapidly
- ii) Resistance once developed can be difficult to reverse and it is high in many low- and low-middle income countries
- Stewardship and disease prevention are important but will not necessarily reverse AMR especially in places with existing high levels of resistance (little or no fitness cost for resistance and multiple drivers of AMR not just use of AMs, co-selection, heavy metals, disinfectants)
- iv) Preventive/control measures for some diseases, other than use of AMs are still not well developed especially for pig production
- v) Experiences from avian influenza demonstrates that improving farm level biosecurity is difficult, especially for smaller scale producers in low and low-middle income countries.
- vi) Vet services remain weak in many countries despite investments in this area (insufficient budget from government and donor funds cannot fill these gaps)

There are limited tools available to mitigate AMR and these may not deliver significant reductions in resistance. These are:

1. Reduce incidence of disease to reduce use of AMs – enhance biosecurity and better use of vaccines and other non-AM interventions.

Note that:

- A number of viral diseases predispose to bacterial infections. Therefore diagnostic testing is complicated so the move towards rapid diagnostic tests as promoted for human health to guide treatment may be less relevant in the food animal production sector.
- For many bacterial and viral diseases, vaccines are imperfect or not readily available or the cost of vaccination exceeds the benefit, especially in low margin settings
- Farm biosecurity is generally poor in low and low-middle income countries and the factors that prevent improvements in biosecurity (including social and economic factors) have been well explored. They are difficult to overcome especially for low margin production systems.

Recommendation

Develop locally appropriate guidance on disease prevention and control based on actual case studies in low and low-middle income countries recognising the constraints to implementation

Continue to work with the private sector to develop improved, affordable vaccines for major endemic diseases of food animals

2. AM stewardship

AM stewardship is an essential element but one that may only have incremental effects on existing resistance

There are no excuses, with existing technology, not to provide access to tailored information on appropriate treatments and control measures for production animal diseases in local language

Recommendation

In all low and low-middle income countries determine whether there are any situations where use of 3rd and 4th generation cephalosporins, fluoroquinolones and other high priority critically important AMs are essential for treatment of diseases.

Develop AM stewardship guidance and resources relevant to local needs in low and low-medium income countries

Note: AM stewardship should be regarded as a tool not an end in itself

To implement these programmes it will be necessary to find ways to overcome the weak veterinary services and existing programmes such as the PVS process are only making slow progress. This process should continue but alternatives that provide immediate support are required. The focus should be on low and middle income countries where levels of resistance are higher and vet services generally weaker.

Recommendation

Explore the option of remotely delivered veterinary support, delivered in local languages, to supplement local veterinary services.

In an age with ready access to mobile phones and internet even in relatively remote parts of many low income countries and high levels of skilled migration from low to high income countries, this should be feasible.

High levels of resistance occur already in Asia. This has already been identified in most countries even if not quantified. Therefore, developing surveillance system to show there is a problem is not the highest priority – we know there is a problem. There is currently too much focus on surveillance and not enough on mitigation and adaptation. There are other indicators that can be used to measure progress other than levels of resistance in selected organisms.

Countries will develop AMR action plans for food animals but based on experiences with avian influenza and other diseases many of these will not be implemented due to lack of resources.

Recommendation

Shift the main focus of support from surveillance programmes to measures that will assist in mitigation and adaptation

Biosecurity is generally poor in low and low-middle income countries and the factors that prevent improvements in biosecurity (including social and economic factors) have been well explored. They are difficult to overcome especially for low margin production systems.

Large companies have and will continue to develop and implement action plans on AMR and AM usage to meet corporate social responsibilities, often derived from consumer pressure

The export sector in low and low-middle income countries must meet importing country requirements (e.g. proposed EC rules on equivalence) but this does not affect production for local consumption

Recommendation

Continue support for building higher biosecurity production and marketing systems for food animals and work with large private sector stakeholders to implement and communicate appropriate AMR policies

Adaptation

Given mitigation will not resolve the problem of AMR it is essential to examine ways to adapt so as to contain resistant organisms and genes (biocontainment)

There are two main pathways for AMR organisms and AMR genes to leave farms

i) Livestock waste treatment (what works, what doesn't and of those that work which ones are affordable?). This should cover removal of residual AMs and AMR organisms and AM genes

Recommendation

Support applied research into methods for livestock treatment building on the existing data already available for treatment of human and animal waste (e.g. composting, bio-char production, filtration, ozone exposure etc.)

Promote the use of measures that are practical and feasible in low and low-middle income countries

ii) Animals that leave the farm (how to reduce resistant bacteria from leaving the farm in animals given these genes/organisms will be present when animals go to slaughter)

This is an area that has not received much attention but there may be lessons to be learned from work on manipulating the microbiome – in particular methods that do not depend on use of AMs (faecal transplants, phages, probiotics, other).

Recommendation

Support applied research into methods that can reduce the number of existing resistant organisms and resistance genes in food animals prior to leaving farms

Other comments

Be careful in introducing another "safeguard" for World Bank projects (viewing projects through an AMR lens) – already the time spent on safeguards can exceed the time spent reviewing the technical merits of project (based on experiences from World Bank projects on avian influenza in 4 countries).

Be careful in developing central advisory bodies that these do not create a "parallel universe" that has little relevance to events at the country level (based on experiences in reviewing UNSIC and the documents it produced with partners from international agencies and the World Bank).

Be careful in developing communication packages that these actually deliver the right, actionable, message(s) especially for a complex issue for which there is no simple solution (based on experiences with avian influenza communications – much of which had little impact in changing behaviours)

Marc Mendelson, Professor of Infectious Diseases, University of Cape Town

From: <u>Marc Mendelson</u>
To: <u>IACG-secretariat</u>

Subject: Feedback on IACG Draft Recommendations

Date: Thursday, February 14, 2019 16:12:28

Dear IACG,

Thank you for the considerable amount of work that has gone into the drafting of these recommendations and to the body of work that brought you to this point. Overall, it provides a sound framework to mitigate AMR. I have 2 specific comments

- 1. Recommendation E4: Despite the complex nature of the arguments for and against binding or non-binding international instruments, and recognizing the primacy of strengthening existing global standards and best practices, I would call upon the UN Secretary General to convene an Expert Taskforce or similar Body to provide a report on the options for long-term adoption of such an instrument or instruments. I don't think that it can be dismissed in the way it is in your draft recommendations
- 2. The draft recommendations identify the critical role that infection prevention plays in driving AMR, and I appreciate the numerous references in its text, calling for more resources for IPC measures. However, I do not think that the recommendations go far enough, nor do I think that they will promote meaningful investment, particularly in LMICs that have little national budget to implement the improvement measures needed. I would like to see much stronger language used in respect to investment into, and attainment of, the provision of safe water and sanitation to citizens of LMICs. I would like to see defined targets expressed in line with SDG6. Moreover, there needs to be accountability of governments in LMICs who do not reach their targets.
- 3. The need to develop and agree metrics for the various interventions that the draft recommends is missing. A metrics unit should be set up to address this issue.

Thank you for the opportunity to comment.

Sincerely,

Professor Marc Mendelson Professor of Infectious Diseases University of Cape Town South Africa

Mark D. Sobsey, Research Professor, University of North Carolina, Gillings School of Global Public Health

From: Sobsey, Mark D.

To: IACG-secretariat

Subject: AMR and WaSH: Greater emphasis on a One Health Appraoch based on microbial data is needed

Date: Wednesday, February 20, 2019 14:41:43

To Whom It May Concern:

What is lacking in this IACG document and more generally is the recognition that without effective human and animal fecal waste management to greatly reduce the concentrations and loads of antimicrobials and antimicrobial resistant bacteria that get into the environment where people and animals get exposed to them, there will continue to be continured high AMR presence and excess environmental exposures that lead to excessive levels of infection, illness, mortality.

Current global efforts on sanitation to address AMR are lacking in will, effective strategies and tools as a global One Health issue. We (e.g., WHO) encourage safe drinking and recreational waters and provide guidance (as drinking and recreational water quality guidelines that have quantitative microbial targets to reduce exposure and health risks). In stark contrast we do not have equivalent actionable targets for human or animal wastes that get discharged into the environment.

Furthermore, in many countries and regions we do not adequately encourage and provide sufficient guidance on environmental surveillance for fecal bacteria and especially AMR fecal bacteria in such fecal waste streams from human and animal sources. Only the recent WHO Tricycle Project seems to have addressed this problem with a One Health approach. However, this effort in being done in the absence of a framework for what levels of AMR fecal microbes in human and animal sources and environmental samples are "acceptable" and pose low risk.

Improvements are needed in human and animal fecal waste management to reduce fecal bacteria, including those that are AMR to very low levels to achieve acceptably low health risks.

A step in the right direction may be the new ISO 30500 Standard for commercial, non-sewered, on-site waste treatment systems that was recently developed. However, this standard is only for commercial, turn-key, rather high-end, on-site sanitation treatment systems that are not likely to be either practical or affordable in the developing world. Therefore, innovative waste treatment and management solutions that can achieve the same microbial performance targets as those in this standard are needed, including those that are either DYI or can be created and implemented without having to be purchased as a system from a foreign commercial source.

There would also need to be on-going monitoring through surveillance to determine if such improved waste treatment and management systems are achieving their microbial performance targets. Such ongoing microbial analysis in low resource settings also needs practical solutions and tools. Currently, it is impossible or unaffordable in much of the world. Even in the USA, no one monitors the microbial quality of drinking water for about 1 of every 5 households because of the lack of a surveillance system or a requirement for one.

Overall, the financial support for any WaSH AMR effort has to be addressed and how such improved treatment and monitoring technology gets financed is beyond me.

Kind regards,
Mark D. Sobsey, PhD
Formerly, Kenan Distinguished Professor and now Research Professor
University of North Carolina, Gillings School of Global Public Health

Member, WHO Guidelines Development Group for Guidelines for Drinking-water Quality Member, WHO AGISAR Member, Science Advisory Board, EU Joint Program Initiative on Antimicrobial Resistance

Michael Ryan, OECD

 From:
 Saija Kalenius

 To:
 IACG-secretariat

 Subject:
 FW: AMR PPT

Date: Tuesday, February 19, 2019 09:46:30

Michael's comments from the Paris meeting for the groups consideration.

Regards,

Saija.

Dear Kimmo, All,

Thank you for hosting the meeting and the invitation to moderate the discussion part. I found the discussions very helpful with several very relevant points raised, which could further be developed and enhance the Draft Recommendations.

On the draft document, I have a few suggestions to help the readability of the report. Overall the paper is relatively comprehensive, but I think it is far too long and somewhat repetitive and a bit convoluted. It could be sharpened and made more succinct and targeted by shortening the paper to about 5-6 pages that highlight the main recommendations of the IACG (perhaps 8-10 points). The detailed text and numerous bullet points could be put in a short annex. This annex could be divided into a number of sections; human health, animal health, plant health and aquaculture.

In addition, the short succinct Draft could be enhanced by adding some carefully selected practical examples, as well as 1-2 graphs or charts. This would help lighten the read, while reinforcing the key messages that come from the consultations.

Thank you Saija for the good summary of the meeting. I have had a chance to reflect a bit more on the meeting, and I have listed a number of points below which you may wish to consider as you prepare the final recommendations.

- -what needs to be done to incentivise good behaviour in the use of antibiotics in livestock production. Generally, farmers respond to both market signals and to government policies.
- -a greater emphasis on the economics, relative costs/risks and access to appropriate and needed antibiotics in livestock production to ensure animal welfare.
- -the potential trade aspects that may arise.
- -a clarification of the linkages between the recommendations at global level and national level.
- -The role of the environment in the transmission of resistant pathogens across and between species.

Thanks again and good luck with finalising the report.

With kindest regards.

Michael

Mohammed Ishaaq Datay et al.

19 Feb 2018

To the IACG Secretariat

Call for securing access to First line Antibiotics such as Penicillin

Dear IACG,

Thank you for this opportunity to make comment on the 'Draft recommendations of the Ad Hoc Inter-Agency Coordination Group on Antimicrobial Resistance'.

We support the majority of the recommendations as laid out in the document. However we call upon the IACG to strengthen the recommended actions to ensure short-medium term access to penicillin in low resource countries with high burden of infection. This 'old' antibiotic is critical for the prevention of Rheumatic Heart Disease (RHD) and the treatment of syphilis. As a result of the global penicillin shortage, pregnant women with syphilis are receiving sub-optimal treatment, and their children are being born with congenital syphilis, with devastating effect.

Similarly, penicillin shortage is hampering public health programs in LMICs to prevent RHD. Penicillin is clearly a critical 1st line antibiotic in the management of numerous other prevalent infections, which are now being treated with broader spectrum antibiotics which drives antibiotic resistance to a greater extent than their narrower counterparts. Hence from an antibiotic stewardship perspective, this is a further compelling argument for focusing increased action to stimulate production of penicillin.

The IACG will be aware of the multiple different reasons for market failure in production of old antibiotics, and we acknowledge that there are already a number of references in the draft recommendations to improving access through suggested national-level interventions. However, we do not feel the recommendations go far enough, and as we see this as an intervention that must not only come from member state governments, but rather as a cross-cutting issue of international concern, we would like this reflected in the document.

As such, we call upon the IACG to include in its recommendations, the establishment of a high-level taskforce under the most appropriate group of partners e.g., UN, Tripartite Alliance, and World Bank, to rapidly accumulate the international demand forecasts for penicillin, and put in place the financing and production measures required to ensure increased production and access to penicillin, targeting, in the first instance, low-resource settings with high burden of infection.

Sincerely,

Dr Mohammed Ishaaq Datay - Specialist Physician and Senior Lecturer PHC and Health Promotion University of Cape Town

Prof Leslie London - Chair of Public Health Medicine and Head of Division, School of Public Health and Family Medicine

Prof Steve Reid - Professor Rural Health and Director of Primary Health Care Directorate UCT

Prof Gary Maartens – Infectious Disease Specialist and Professor of Clinical Pharmacology, University of Cape Town

Prof Mpiko Ntsekhe - Chair of Cardiology, at the University of Cape Town

Sarah Davids - People Health Movement

Dr Tasleem Ras – Specialist Family Physician and Senior Lecturer Division of Family Medicine University of Cape Town

Prof Marc Blockman – Associate Professor Division of Clinical Pharmacology and Chair of Human Research Ethics Committee University of Cape Town

Prof Ntobeko A.B Ntusi – Cardiologist and Professor of Medicine, Head and Chair Department of Medicine, University of Cape Town

Prof Sipho Dlamini - Associate Professor, Division Infectious Disease & HIV Medicine, Department of Medicine, University of Cape Town

Dr Ismail Bandeker – Specialist Physician and Senior Lecture New Somerset Hospital and University of Cape Town

Dr Charle Viljoen - Specialist Physician and Cardiology Fellow, University of Cape Town

Nobuko Ichikawa & Matthias Loening

OFFICIAL USE

Feedback to Draft Recommendations of the ad hoc IACG on AMR (February 2019)

Thank you for the opportunity to provide feedback to the draft recommendations.

Nobuko Ichikawa, senior environmental advisor of the European Bank for Reconstruction & Development (EBRD) has participated in WHO's development partners' meeting on AMR in June 2018 as well as Wellcome Trust-hosted IACG Recommendations private sector-focused consultation meeting on February 7th, 2019. Below is feedback from Matthias Loening (senior health sector advisor) and Nobuko. Please note that our feedback does not necessary represent EBRD's views but are based on our professional experience and knowledge.

- 1. We echo the view in A1 that both equitable and affordable access and prudent use of antibiotics as well as urgency and One Health are emphasised.
- 2. Page 3, it would be good to consider recommending ensuring implementation of best practices, local and international quality assurance guidelines to ensuring quality assurance in health care services
- 3. Page 4, the third bullet pint "Establishing antimicrobial production facilities: Some governments or regional entities may consider establishing production facilities". We wonder if this is the role of the government as well as feasible. Investment decision of production facilities of antimicrobial is likely to be made by a private firm. Moreover, most shortages are not due to lack of production but rather local supply chains. Strengthening supply chains should be mentioned.
- 4. Page 5, the first bullet point under Considerations for this recommendation: A quarter century ago, international organisations promoted National Environmental Action Plan for the developing countries. Unfortunately, these action plans tended to end up in the shelves where governments lacked institutional and financial capacities. Spelling out the action plan can be concise could be practical.
- 5. Page 6, the Highest Priority Critically Important Antibiotic Agents in the shaded box: We hear that European Medicines Agency (EMA) and EU are developing its own critically important antibiotic agents (CIAA), respectively. Is it possible to have <u>One Set of CIAA</u> to avoid any confusion?
- 6. Page 7, a. ...the most important research... in the shaded box: In a meeting of the British Association for Antimicrobial Chemotherapy, we heard views to support relatively wider coverage of support on AMR research instead of very targeted. Perhaps this is due to the possibility where success of innovation could possibly come from non-targeted basic research as well. There is also a question who decides where should be targeted. Therefore, instead of "strategically targeting the most important research" it may be considered to be "Financial and non-financial incentives strategically *involving best scientific talents and institutions to take up AMR* scientific challenges, and ..."

- 7. Page 7, the last bullet point: The Global Health Innovation Technology Fund may be considered to be added to the list of the existing international mechanisms. GHIT is a public-private partnership fund for global health R&D. We invest in nonprofit product development for HIV/AIDS, malaria, tuberculosis, and NTDs. Our funding partners, including the Government of Japan, Bill & Melinda Gates Foundation, Wellcome Trust, and global life sciences companies, have committed more than \$200 million for the second phase of GHIT's operations (FY2018- FY2022).
- 8. Page 9, lack of data is a huge problem. Recommendations should support not only data but key common metrics for data sharing and monitoring.
- 9. Page 10, bullet point a: "Welcoming" could be used instead of "strengthen" as some government and entities seem to have reluctance to listen to the civil society voice in general. Their role is critical for AMR in the same way as climate change. They are a driving force.
- 10. Page 11, invest for a sustainable response, possibly rather than suggesting more financial resources are needed, state that investing in AMR intervention is a good return on investment for governmental, non-governmental, private sector and donors (OECD: Stopping AMR would cost just \$2 per person a year).
- 11. Page 11, the shaded box.: We would recommend additional bullet points "Promote industrial best practice by quality control all in the relevant sectors involving production, distribution and use of antibiotics and protein products affected by antibiotics use." We would also suggest to revise "c". into two bullet points: "Engage by the private sector in collaborative efforts to collect, analyse and use date" and "Work with the private sector to devise, pilot and scale up financial and non-financial mechanisms to move from volume sale business model of antibiotic to a value, quality and sustainability business model" and "d. Contributions to addressing...." to "AMR risk scenario analysis and management in investment decisions by institutional investors, asset managers and banks for its investment decisions by environmental, social and governance responsibility and business sustainability".
- 12. Page 11, The relevant private sector actors and influencers on AMR issues could be listed such as pension fund, asset managers, banks, health insurance, restating chains, Protein producers, food distributors, pharmaceuticals, private health care services, medical technologies, rating agencies and accounting firms, e-commerce and media
- 13. Perhaps a shorter version of the document could be user friendly. One specific area you may consider to create is a media strategy. There have been highly educational programmes on AMR produced to date. Outreaching AMR knowledge in such programme could be effective. Beside SNS & mobile device could be strong tools to spread AMR knowledge. Young generation could be a force to fight against AMR.

Peter Collignon, Infectious Diseases Physician and Microbiologist, Canberra Hospital

From: Collignon
To: IACG-secretariat

Cc: ""Peter Collignon"; Collignon, Peter (Health)

Subject: Comments on the draft recommendations of the ad hoc inter-agency coordination group on antimicrobial

resistance

Date: Tuesday, February 19, 2019 23:59:51

Attachments:

Overall these recommendations and their context, are a welcome step forward to better control antimicrobial resistance (AMR) globally. They incorporate the "One Health" concept. Thus, they are looking at not only the use of antibiotics in people, but also what is happening in at food animals and the environment. General issues are also addressed, particularly the issues of water and sanitation.

My main reservation is that the predominant emphasis still seems to be on antibiotics i.e. the control of antibiotics and the development of new antibiotics. While obviously the this is a very important issue, if we want to better manage antimicrobial resistance and if we fail to adequately address how resistant bacteria and their genes spread, we will not be able to adequately manage this problem.

Infection prevention and control in its broadest sense is vitally important if we want to stop the spread of resistant bacteria. The spread of resistant bacteria is likely the major factor accounting for the very high levels of AMR we see in many regions. This is not just in the healthcare setting but in the community. It is also the most likely explanation for the very large differences in AMR rates seen between different countries.

On a global perspective the biggest factor in the spread of resistant bacteria in their genes is likely to be poor water quality and inadequate sanitation. Other infrastructure issues such adequate housing, electricity supply etc are also important issues, but given the large number of studies showing high levels of contamination of waterways with resistant bacteria (e.g. carbapenem resistant E.coli), obviously water and sanitation needs to a major focus. This is not only an issue for people but also for food animals, because water carrying resistant bacteria is used in and between these various sectors and the environment. Other issues to do with water will be the levels of different antibiotics, contaminants and drugs that may be present.

We recently did a study where we looked at factors that might explain the major differences in antimicrobial resistance levels between various countries globally (attached). This clearly show that poorer infrastructure (for example water and sanitation) was the largest factor in explaining the major differences in AMR rates seen between countries. Another major factor was governance (e.g. corruption levels). Surprisingly differences in antibiotic volumes used in people, did not explain the differences seen between countries.

Therefore, I think it would be useful if these issues (that a very different to antibiotic use and new drug development), could be better emphasized in the recommendations and associated comments.

The current recommendations seem mainly to be focused towards better controlling the use of the antibiotics we already have, and the development of new ones. These are all very worthwhile, but

issues to do with the spread of infection are not given the same prominence. It would be nice if there could be added extra recommendations emphasizing better controls on the spread of resistant bacteria — and particularly by water and in waterways. It is also important that adequate funding to achieve this is recommended. If making new recommendations is too difficult at this stage of the consultation process however, then I think sanitation and water issues should be better separated in the comments to be more stand alone when associated with the current recommendations

In particular, I think this pertains to recommendations A1, A2, B1 and B2. There also need more focus on obtaining the adequate water and sanitation for globally for all people. So financing, when it is implied or stated in recommendations C2 and D1, needs to emphasis water and sanitation as priorities.

Under accountability in global governance and recommendation E1, I think it's important that we better emphasize the need for good governance (e.g. better control on corruption, rule of law etc) if we want to achieve lower antibiotic resistance rates. If globally we don't improve and have better governance in place, then all the necessary tools to control the use of antibiotics and stop the spread of resistant bacteria (e.g. thru good infrastructure etc) are less likely to occur or be effective.

In summary I think the approach of the Ad Hoc group by using the "One Health" context is excellent. However, my concern is the focus is still overwhelmingly and predominantly on antimicrobial stewardship and new antibiotic production (including research priorities and the financing of this of new antibiotics). These are very important, but that if we don't better emphasize and prioritize controls on the major ways that antibiotic resistant bacteria and their genes spread, then we will likely fail to better manage the ongoing rapid spread of resistant bacteria,

These are my individual comments and not those on behalf of any of my organisations, although I believe both my health authority and university would strongly support what I have stated. I have been a member of many expert panels and groups dealing with AMR for WHO as well as in Australia including as chair of many committees, for over 20 years.

Peter Collignon AM Infectious Diseases Physician and Microbiologist, Canberra Hospital Executive Director, ACT Pathology.

Professor, Medical School. Australian National University.

The author has no conflicts of interest to declare.

Saving antibiotics in a carbon-constrained world

Actionable recommendation: The social cost of carbon is an unaddressed barrier to equitable access to antibiotics for future generations. Thus, global antimicrobial resistance (AMR) policy can explicitly incorporate environmentally sustainable procurement and emphasize regional leadership models that enable digital participation.

Recommendation C1 highlights ways to mainstream AMR into the agenda of other contemporary issues. However, a relevant response to AMR is also sensitive to the issues relevant to our times. Both climate change and AMR are recognized as threats to global health by the World Health Organization (1). In fact, UN Secretary General Antonio Guterres said that "Climate change is the defining issue of our time" (2). The social cost of carbon represents a real challenge to maintaining equitable access to antibiotics for future generations (3). Nonetheless, the draft recommendations and its One Health perspective lays an excellent foundation for crafting the antibiotic stewardship policy of a carbon-constrained reality.

Recommendation A1 identifies improved procurement by creating local antimicrobial production facilities. This is compatible with a sustainable procurement framework. Sustainable procurement with respect to emissions not just finances is a means to ensure inter-generational equitable access to antibiotics. For example, in Tajikistan, 82% of the carbon footprint of UNDP-administered Global Fund for HIV/AIDS and Tuberculosis projects came from the supply chain (4). The UN Informal Committee on Sustainable Procurement or the UN Initiative on Greening Procurement in the Health Sector have produced documents that could be drawn up to explicitly incorporate sustainable procurement into **Recommendation A1**.

Recommendation E1 highlights the need for a One Health Global Leadership Group on Antimicrobial Resistance, a partnership platform for global coordination and an Independent Panel on Evidence for Action against Antimicrobial Resistance ("proposed groups") These proposed groups will undoubtedly be invaluable in addressing AMR. It is encouraging to see regional models for technical cooperation and coordination emphasized in **Recommendation E3**. Under a regionalized model, the proposed groups can improve stakeholder involvement by allowing meaningful digital participation. The discussions will benefit from the potentially new faces and hopefully new ideas. The technology exists. Several sessions of the Wellcome Trust's Call to Action against drug-resistant infections in November 2018 were livestreamed. However, a hybrid offline-online model is likely favourable (e.g. one central node and several distal nodes for one meeting and/or initial face-to-face meeting and subsequent online meetings).

"Antimicrobial prescribing is performed in an environment where the behavior of clinical leaders or seniors influences practice of junior doctors." Global antimicrobial stewardship policy is no different. Flying is deeply embedded within global health's culture and practice. Many notable academics have recognized the waste associated with frequent flying (5). As an early career researcher, I wonder whether One Health is compatible with frequent flying? Would flying less reduce one's influence and ability to address AMR? The next generation of scientists, clinicians and policymakers for AMR are modelling their careers on your response to these questions.

The partnership platform: who, what proportion and why?

Actionable recommendation regarding Recommendation E1: The partnership platform should pay special attention to the composition of various groups through a transparent process. The response to AMR will benefit if civil society is better represented in the platform.

The recommendation on the partnership platform encourages various stakeholders to work together to craft global and country goals that are meaningful. As political support for solutions to AMR increases and potential legal instruments for global stewardship are pursued, the history and dilution of the Millennium Development Goal-1 for extreme poverty and hunger becomes especially salient. Methodology rather than policy enabled the "achievement" of MDG-1 in 2015 (6). Careful attention to the partnership platform's composition can hopefully prevent a similar scenario for AMR.

The partnership platform would benefit from a transparent selection criteria and selection process. Presently, civil society is less represented than the private-sector within similar global health platforms (7). Current norms for composition are not evidence-based and the response to AMR can be made more robust by giving civil society partners better representation than is typical.

References

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- 7. Storeng KT, Puyvalle ADB. Civil society participation in global public private partnerships for health. 2018;(August):928–36.

Response to:

<u>Draft Recommendations of the Ad-Hoc Inter-Agency Coordination Group on Antimicrobial</u> Resistance

By:

Professor Sabiha Essack (B. Pharm., M. Pharm., PhD)
South African Research Chair in Antibiotic Resistance and One Health
Antimicrobial Research Unit, University of KwaZulu-Natal, Durban, South Africa

Responding as an Individual

The following are my recommendations on the different areas covered in the draft document with amendments indicated in red font where appropriate.

Preamble:

 Antimicrobial resistance (AMR) should be explicitly linked to the sustainable development goals (SDGs), universal health coverage (UHC) and climate change in the preamble.

A1:

- Add a recommendation on regulatory mechanisms to ensure that antimicrobial medicines registered for use in humans, animals and plants are of proven quality, efficacy and safety.
- Amend (d) to read: Supporting behaviour change through effective communication and incentives socio-behavioural interventions targeted at.....
- Under "Considerations for this recommendation", expand "addressing shortages and stockouts" to include the continuum of supply chain management from manufacture of the active pharmaceutical ingredient to safe disposal of expired or unused drugs.
- Add a consideration related to leveraging and aligning AMR-related aspects contained in the UN Political Declaration, the Global Action Plan on AMR, the International Health Regulations (IHR) and the Global Health Security Agenda (GHSA)

A2:

- Under "Considerations for this recommendation" amend bullet 2 to read: "Furthermore such differences between Countries should, within their particular contexts and resource constraints, inform and help to define"
- Add a consideration related to the importance of taking an integrated systems approach
 to preventing and containing AMR by means of a social compact that suspends sectoral
 interests for the good of public health.
- The 4th bullet should move to A1 as it speaks to interventions at global level

A3:

 Add a consideration related to the improvement of animal husbandry to allow the incremental removal of priority antibiotics for growth promotion, prophylaxis and metaphylaxis.

B1:

• Include academia as a key role player in research and development.

B2:

• Remove bullet 2 – it is a repeat of bullet 1.

B3:

 Research should encompass the biomedical, clinical, socio-behavioural and policy aspects of AMR as opposed to the focus on the resercah and development of new drugs, diagnostics and antimicrobial alternatives.

D1:

• AMR should be explicitly linked to the SDGs, UHC and climate change.

D2:

• The importance of leveraging domestic funds from AMR-specific and AMR-cognate programmes should be included here.

E1:

 Amend (a) to read: "Maintain urgency, public support, political momentum, mobilization, advocacy and visibility ..."

E3:

- Amend the recommendation to read: "The IACG requestsby enhancing their organizational capacity, adopting an integrated systems approach and providing adequate"
- Under "Considerations for this recommendation" under bullet 2, consider adding that the initiatives of the tripartite + at global level should be cascaded to regional and country levels.

Other:

• Surveillance should encompass both antimicrobial use and antimicrobial resistance in all three of the human, animal and environmental health sectors.

Wendy Thompson, Doctoral Research Fellow, University of Leeds

From: Wendy Thompson [RPG]
To: IACG-secretariat

Cc: Susie Sanderson; SPRENGER, Marc

Subject: Feedback on draft IACG recommendations on AMR

Date: Saturday, February 2, 2019 14:15:03

In response to your consultation on: DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE dated Jan 2019, please see below my request for the addition of one word.

Respondent: Wendy Thompson, Doctoral Research Fellow, University of Leeds, UK - responding as an individual

- Background With dentists responsible for around 10% of all antibiotic use in global healthcare (source: FDI, 2017), I would like to see dentists explicitly mentioned in the list of clinicians. Global dental antimicrobial stewardship (AMS) is in its infancy relative to other areas of healthcare. The addition of this one word would provide significant leverage for increasing the profile of this important aspect both within the global dental community and across healthcare.
- Feedback: At the bottom of page 4: 'The prudent use of antimicrobials including physicians, dentists, pharmacists,'.

Reference: FDI(2017) - https://www.fdiworlddental.org/news/20170213/dentists-should-be-consulted-about-amr-fdi-tells-who

Dentists should be consulted about AMR, FDI tells WHO | FDI World Dental Federation

www.fdiworlddental.org

Invited to comment on a report by the Secretariat of the World Health Organization (WHO) on antimicrobial resistance (AMR), FDI highlighted that dentists are among the major prescribers of antibiotics, estimated at between 7–11 % of all antibiotic prescriptions, depending on the country.

Thanks in advance Wendy

Wendy Thompson
NIHR Doctoral Research Fellow & General Dental Practitioner

Gavi, the Vaccine Alliance

From: <u>Wilson Mok</u>
To: <u>IACG-secretariat</u>

Subject: Feedback on draft recommendations **Date:** Saturday, February 2, 2019 12:23:31

Attachments:

Dear IACG Secretariat,

Please find below feedback on the draft recommendations.

- In section B it would be helpful to see an acknowledgement of the need to have better evidence and tools (e.g., data on AMR burden; epidemiological/impact modelling) as an enabler of the R&D and downstream investment decisions that we would like to see. This is one of the underlying issues that may either hold back investment (not being able to make a strong investment case) or hold back more robust prioritisation and allocation of limited resources across many different potential AMR-associated investment options (different pathogens, different types of technology for a given pathogen)
- Sections B and D both speak to the need for increased investment but I think there could be better coherence and clarity across the two sections. For example, it seems Section D focuses on investment at the domestic level (including funding national plans), but quite general language is used around need for investment that it isn't quite clear what the focus of the recommendation is. The Fleming Fund is referenced in this section, when it would seem their contribution is more linked with innovation (Section B). And organisations like Gavi and GF, which span both commodity/product and systems funding, are called out in both sections, so particularly important to be precise on what is being asked in each instance. As another example, I would argue that recommendation B2 around leveraging existing mechanisms like Gavi for delivery of new innovations could go a step further to say that these actors prioritise AMR-relevant products (e.g., vaccines) in investments; that message does come across in D, but there it's more focused on funding to countries.
- In B1 there are a couple instances of language appropriate for antibiotics, but not vaccines and diagnostics even though all three technologies are part of the recommendation. For example, in the recommendation all three types of products are categorised as "new antimicrobials", which is awkward. Later, the word "compounds" is used in regards to R&D cost and success rate; a more generic terms should be used instead to also be applicable to vaccines and diagnostics.

Best regards,
Wilson Mok
Head of Policy
Gavi, the Vaccine Alliance

Wilson Mok

Head, Policy Vaccines & Sustainability



Global Antibiotic Research & Development Partnership (GARDP)



The Global Antibiotic Research & Development Partnership's comments on the Draft Recommendations of the Ad Hoc Interagency Coordination Group on Antimicrobial resistance (IACG)

The Global Antibiotic Research and Development Partnership (GARDP) is a not-for-profit research and development organization that addresses global public health needs by developing and delivering new or improved antibiotic treatments, while endeavoring to ensure their sustainable access. Initiated by World Health Organization (WHO) and the not-for-profit Drugs for Neglected Diseases initiative (DNDi) in May 2016, GARDP is an important element of WHO's Global Action Plan on Antimicrobial Resistance that calls for new public private partnerships to encourage research and development of new antimicrobial agents and diagnostics. GARDP's programmes — sexually-transmitted infections, neonatal sepsis, paediatric antibiotics and antimicrobial memory recovery, evaluation and exploratory research — are designed to address global public health priorities. Each programme incorporates sustainable access and stewardship strategies to ensure treatments are affordable and available to all those who need them.

GARDP welcomes the opportunity to comment on the draft recommendations prior to finalization, and as part of sustained effective global action to address antimicrobial resistance, the recognition by the IACG of the need to address innovation and access to existing and new health technologies.

GARDP's response focuses on R&D for human health, while recognizing and supporting the need for better prevention of infections in humans and animals, a One Health approach, and the potential for synergies between approaches taken.

General comments

A global, collective and coordinated effort is required to tackle the many challenges related to delivering effective, appropriate and affordable antibiotic treatments. The recommendations address several of these challenges. However, to strengthen the impact of the recommendations, GARDP encourages the IACG to consider further developing and including the following additional points in the final recommendations:

• As a general point, to retain focus on the greatest threats to human health, it is important that the recommendations on R&D, including on access, reinforce the point made in the introduction that drug-resistant infections caused by bacteria, viruses, fungi and parasites all need to be addressed. A specific mention of the WHO's "priority pathogens" list¹ of bacterial species that cause infections for which there is the greatest need for new antibiotics, and so pose a great threat to human health, should be included. The list was drawn up to guide and promote research and development of new antibiotics and highlights the threat of drug-resistant infections by Gram-negative bacteria that are outpacing drug discovery at an

 $^{1} \qquad \text{https://www.who.int/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed}$

alarming rate. As shown in the recent WHO pipeline report², the current clinical pipeline for new antibiotics is sparsely populated and in addition to already identified priority needs in TB does not adequately reflect global public health priorities.

- The IACG could encourage the development of R&D roadmaps for priority drug-resistant infections in priority patient populations. GARDP suggests the IACG, as part of this work, address the significant gap between initial regulatory approval and the evidence needed to support treatment decisions at a patient and public health level, for more complicated or drug-resistant infections. For example, in sexually transmitted infections, GARDP with the support of WHO and global experts, is developing an R&D strategy for STIs that addresses the need for an aligned regulatory and public health pathway.³
- The IACG recommendations focus on different elements of the response to antimicrobial resistance, such as national plans, and on surveillance. These and other essential aspects such as infection prevention and control, and public awareness raising are also relevant for R&D. Developers need to take into account the diversity of national health systems challenges, national plans, and levels of economic development. Surveillance activities not only serve epidemiological purposes but should link to R&D efforts in a mutually reinforcing way country or regional-specific R&D programmes should address the drug-resistance profiles and can feed back into surveillance efforts. It is therefore important that the IACG, as part of its review of each element, recognizes that there are overlaps between them, and that in its final recommendations, seeks to ensure coherence both within and between recommendations, including by cross referencing linked activities.

Specific Comments

Recommendation A1: GARDP strongly supports the call for all Member States to ensure both equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use.

GARDP suggests as there are few international standards for human health, that there is a cross reference to, **recommendation E4** that the Tripartite group should expedite its work, including consideration of potential new, binding or non-binding international instruments. GARDP argues that such instruments **must**, not **may** include a stronger focus on supporting the distribution and appropriate use of existing and new antimicrobial medicines, diagnostics, vaccines and other interventions, while also preserving existing antimicrobial agents, including using the WHO ACCESS, WATCH and RESERVE categorization of antibiotics.

Rationale

A1 e) recommends 'Developing national instruments based on international standards for equitable access to and prudent use.' Access and stewardship are also referred to in three other main areas in the recommendations. B2, in relation to Global access initiatives, C2 in relation to enhanced action by the private sector and E4 in relation to the Global Development and Stewardship Framework to Combat Antimicrobial Resistance.

² Antibacterial agents in clinical development: an analysis of the antibacterial clinical development pipeline, including tuberculosis. Geneva: World Health Organization; 2017 (WHO/EMP/IAU/2017.11). Licence: CC BY-NCSA 3.0 IGO. Available at:

http://www.who.int/medicines/news/2017/IAU AntibacterialAgentsClinicalDevelopment webfinal 2017 09 19.pdf?ua=1

³ https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002366

While national instruments are critical to reflect the national context, there needs to be greater recognition in all these recommendations that there are few relevant international standards for human health and that there is an urgent need to accelerate work in this area.

Access and stewardship are integrated as early as possible in the GARDP's development process, including in partnership agreements with industrial partners. While developers can and should play a part in sustainable access, there remains a crucial role for governments, WHO, and other agencies to set the appropriate polices and standards at the national, regional, and global level.

There is an urgent need to move the discussion about access and stewardship from principles to practice, where all stakeholders have a critical role to play; this includes the Tripartite Plus. This should be an important part of the Global Development and Stewardship Framework to Combat Antimicrobial Resistance .

In addition, GARDP suggests

 The IACG should consider making recommendations to support optimization of existing drugs to ensure healthcare professionals have the evidence and the tools to appropriately treat the patients with serious drug-resistant infections.

Rationale

Optimizing the use of existing drugs is critical to protect the efficiency of such drugs over time. This can be achieved by improving the use of old and existing drugs through supporting optimal dosing strategies, generating evidence-based treatments for important diseases and syndromes with bacteria as causative agents, and introducing appropriate diagnostics to guide selection of the most appropriate agent. The IACG should consider making recommendations to support such development. Unfortunately, there is little interest to support downstream development in this space. While it remains a fact that it is more expensive to use most diagnostic tests than prescribe a drug, economic incentives will also be necessary to ensure that such tools are used to guide treatment decisions.

 In addition, to the general suggestion that Governments or regional entities consider building strategic production networks, GARDP suggests that the IACG recommends reviews of specific areas of production capacity. This should include active pharmaceutical ingredient (API) production. Such reviews could include market analyses of key antibiotics (including those on or of interest to the essential medicines list - EML) to identify gaps and liabilities around API and finished drug product manufacturing.

Recommendation B1: GARDP recommends that the IACG consider the full wording of the UN Political Declaration on AMR.

Rationale

GARDP supports the recommendation's emphasis on the need to promote equitable and affordable access to and stewardship of new health products, and that that all 'financial and non-financial incentives.' (should be) 'based on the principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance.'

However, it is important that the IACG take into account the full wording of the UN Political Declaration on Antimicrobial Resistance, which also recognized that 'all research and development efforts should be needs-driven and evidence-based' as well as guided by the principles of affordability, effectiveness and efficiency and equity, and should be considered as a shared responsibility.' and that there is 'a public return on the public investment on R&D.'

The Declaration also acknowledged the importance of reactivating the R&D pipeline through incentive mechanisms that avoid the reliance on the traditional price/volume combinations and the need to

promote appropriate use of antibiotic by 'delinking the cost of investment in research and development on antimicrobial resistance from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools, vaccines, and other results to be gained through research and development.' For this to be implemented, alternative incentive and reimbursement models are needed.

Meeting global health needs means developing drugs aimed at not only targeting priority pathogens (as designated by WHO in their Priority Pathogen List⁴) but also meeting the needs of specific high-risk populations (such as new born babies) and treating under-served diseases and syndromes. This ensures that any new health tools are designed from the start to address priority needs. GARDP's choice of initial programmes follows from these principles and has been supported by expert reviews and input from the World Health Organization (including priority pathogens, pipeline and landscape analyses). If addressing antibiotic resistance is a shared responsibility, and solutions to contain antibiotic resistance are to make a difference globally, then low- and middle- income countries must be part of developing them, so solutions are developed by, with and not just for these countries.

In addition, GARDP suggests:

- The IACG clarifies that a combination of ways to apply (push) and attract (pull) financial investments in R&D will be required to effectively stimulate antibiotic innovation and development. The IACG could encourage pilot models for pull mechanisms which contain enforceable conditions to ensure a public return on investment.
- The IACG adds to the recommendation to highlight the need to also identify the most appropriate private or public sector actors, which in turn should then drive the type of funding approach adopted.
- GARDP thanks the IACG for its acknowledgement of the important role GARDP and other
 existing international mechanisms have in human health, and the need for full and sustained
 funding for such initiatives. Significant and sustained funding is vital if GARDP and others are
 to deliver the new antibiotics and tools needed for the future.
 - GARDP has secured approximately 25% of its initial forecast of EUR 270 million to 2023 to deliver up to four new antibiotic treatments and a robust pipeline of new candidates. It would be helpful for the IACG to underline that funding needs to be available across the development pipeline for new treatments addressing both priority pathogens and populations.
- The IACG should consider a specific recommendation calling for support for existing and the development of further clinical trial networks.

Rationale

The IACG considerations for recommendation B1 discuss 'pulling new products through to markets.' If R&D is to go from' bench to bedside', a combination of ways to apply and attract financial investments in research and development ('push and pull incentives') are likely to be required to effectively stimulate antibiotic innovation and development. GARDP suggests that the IACG makes this point more clearly. Both 'push and pull' mechanisms can be designed for different actors, non-and for profit, and for stages of development. For example, 'push' can be used to take products through to markets, as shown by the successful track records of delivering, recommending, and implementing new treatments has been by the product developers DNDi and Medicines for Malaria

⁴ Antibacterial agents in clinical development: an analysis of the antibacterial clinical development pipeline, including tuberculosis. Geneva: World Health Organization; 2017 (WHO/EMP/IAU/2017.11). Available at: http://www.who.int/medicines/news/2017/IAU Antibacterial Agents Clinical Development webfinal 2017 09 19.pdf?ua=1

Venture (MMV), which are primarily funded by up front 'push' payments. The need for appropriately designed and focused pull mechanisms to complement push incentives remains urgent.

However, focusing solely on types of financial incentives ('push and pull') is not the most appropriate way to frame the issue. Importantly, the IACG recognizes the crucial need to identify at which stage in the R&D pipeline funding should be focused. GARDP suggests adding to this point in the recommendation and highlighting the need to also identify the most appropriate private or public sector actors, which in turn should then drive the type of funding approach adopted. For example, much of the current innovation in the field of antibiotics takes place in academia and in small and medium enterprises (SMEs), incentives need to be designed to meet their needs.

To ensure a public return on public investments, any pull incentive should include a contractual relationship between payer(s) and recipient(s) with strong governance, definitions around what constitutes innovation (based on public health priorities), and a clear agreement on sustainable access. Pilot models would be useful in the short term.

GARDP thanks the IACG for its acknowledgement of the important and encouraging role of existing international mechanisms in human health. This includes GARDP and others such as CARB-X, the REPAIR Fund, Innovative Medicines Initiative, Joint Programming Initiative on Antimicrobial Resistance (JPI-AMR) and the Coalition for Epidemic Preparedness Innovations (CEPI)) and its recommendation for full and sustained funding for such initiatives. Funding needs to be available across the development pipeline for new treatments addressing both priority pathogens and populations is new tools are to are to be brought to patients.

There is still a serious lack of funding for upstream early discovery, pre-clinical and clinical development of antibiotics including the conduct of both regulatory and post regulatory evidence generating clinical trials. The latter is important as regulatory requirements and financial constraints for a new drug to treat multi drug-resistant infections may drive development for certain 'gateway to approval' indications (such as complicated urinary tract infections) via one adequately well controlled study but with a lack of certainty that additional investigations in the indications for infections due to the relevant MDR bacterial species will follow.

Ultimately, there is a lack of new antibiotics recently launched, or in development available to treat infections by the WHO listed priority pathogens in priority patient populations, with paediatrics being the population significantly impacted. Only an estimated 38 percent of antibiotic paediatric development programmes are completed within seven years of adult registration. GARDP's globally-focused programme aims to develop antibiotics for patients with a high burden of drug-resistance – for use in hospitals and the community – in both low- and middle-income countries and high-income settings, and to develop the evidence needed to ensure regulatory approval.

Building research networks globally including clinical trial networks that can integrate drug and diagnostic development is crucial to address more rapid approval of new antibiotics and provide evidence to support treatment decisions. This needs to be done while ensuring country level ownership. While there are important existing initiatives such as the European Developing Country Clinical Trials Partnership (EDCTP) and there is a need to avoid duplication in the areas focused on, additional investments are needed both in developing and developed countries. The IACG should consider a specific recommendation calling for support for existing, and the development, of further clinical trial networks.

GARDP is actively working with countries and existing partners to develop such a network, a platform for paediatric antibiotic development, and additional support is needed both at country and at a

coordination level to build this capability and capacity. ⁵ The platform will collaborate and build partnerships with institutions and experts from across the world to systematically assess and develop new and re-purposed antibiotics for children of all ages. This international platform of experts and clinical trial sites will include the development of innovative trial designs to ensure it is possible to conduct both regulatory clinical trials and including broader public health evidence generating trials, wherever they are needed.

Recommendation B2: GARDP suggests:

- GARDP supports the IACG recommendation on global access initiatives working on AMR need
 to promote and support equitable and affordable access to existing and new antimicrobials,
 diagnostics, vaccines. However, GARDP suggests that the IACG should emphasize that for
 antibiotics, unlike other drugs, widening access must be linked to ensuring that they are used
 only to treat a bacterial infection.
- There may be some possibility to leverage existing global access and scale up initiatives in human health (such as CEPI, GAVI, the Global Fund, Medicines Patent Pool and UNITAID). However, the IACG needs to give greater recognition that many of the challenges in addressing antibiotic resistance are outside of their disease-specific experience. Critically, given their existing mandates, none of them address infections caused by the Gram-negative priority pathogens. They may not necessarily have, or wish to obtain, the expertise needed. In addition, the need to ensure both access and appropriate use can present a series of challenges to existing market shaping approaches. GARDP agrees with the IACG there is also a need to develop new global initiatives and approaches, but these will also need dedicated funding streams for AMR at the national, regional and international level.
- The IACG highlight that access and appropriate use considerations need to be built into the R&D process from the start, including through the use of clear target product profiles (TPPs) that consider the needs of the patients and the characteristics of the relevant health system.
- The IACG should recommend that public and philanthropic funders of R&D consider how suitable contractual measures (including through licensing agreements) can be put in place with public and private -sector actors receiving public support. This may enable both public and private sector actors to successfully and suitably roll out new treatments in the future. Not-for-profit drug developers can play a role in implementing such conditions. For example, partnerships are key to GARDP's programmes and it has been possible to include contractual arrangements with pharmaceutical companies, research institutions, and academic partners that secure freedom to operate and ensure affordability and appropriate use of any new products developed.

Recommendation B3: GARDP agrees that collaboration between all existing and new AMR R&D related initiatives is essential to maximize the effort directed towards stimulating R&D for new antimicrobials in the fight against multi-drug resistance and that openness and transparency on data

⁵ On 3 July 2018 in New Delhi GARDP launched an observational study which is being carried out in hospitals/neonatal units in Bangladesh, Brazil, China, Greece, India, Italy, Kenya, South Africa, Thailand, Vietnam, and Uganda. The study focuses on collecting clinical information on babies with significant/clinical sepsis. It will generate a robust evidence base on how neonatal sepsis is managed which can be used as a basis for evaluating interventions in information be here. future neonates. More can found https://www.gardp.org/2018/newsresources/press-releases/researchers-gather-new-delhi-kick-off-studynewborns-sepsis/

should be promoted and to avoid duplication. GARDP supports and encourages the IACG to identify new ways for the private sector, and those that fund drug development, to share data.

Recommendation C1: GARDP supports the recommendation for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels, and the provision of political, financial and technical support for them to do so. In addition to general advocacy and awareness raising, it is important to highlight the role that civil society groups can, and should, play including in priority setting; financial incentives linked with public health benefits, and supporting national and international mechanisms that ensure delivery, access, availability and stewardship of new and existing health technologies.

Recommendation D2: GARDP supports the IACG's emphasis on the need for increased investment in the global response to antimicrobial resistance and for greater priority to antimicrobial resistance in resource allocations. GARDP suggests that the IACG should recommend calls for countries to explore and critically appraise ways to mobilize new sources of public and private funding at the national, regional and global level. There should be further evaluation, however, before expanding the mandate of existing financing mechanisms in human health (such as Global Fund, GAVI and UNITAID).

Rationale

While GARDP shares the view that existing human health financing mechanism such as the Global Fund, GAVI and UNITAID can contribute to financing access to health technologies for low income countries. Some caution and further evaluation is needed, particularly if there are attempts to expand their mandates. If applied strategically, their institutional experience and skills could provide added value in key areas of AMR R&D, both by their own interventions and by encouraging and leveraging partnerships with others. However, any extension of mandate would need to come with additional funding, so as not to distract from the fulfillment of their existing mandates, and to ensure that funding is not diverted from existing AMR initiatives. Funding to AMR dedicated mechanisms may be an alternative option.

As the IACG notes, these initiatives primarily focus on low income countries, and in addition to those countries that are outside their remit, there are already access and funding challenges for countries that are 'transitioning'. In addition to incentives that apply such funding, GARDP suggests that the IACG should recommend calls for countries to explore and critically appraise ways to mobilize new sources of funding at the national, regional and global level. This could include proposals for taxes such as the pay and play model suggested in the UK AMR Review (O'Neill) report, social impact bonds, development bank funding, and funding, both in cash and in-kind from additional countries to the traditional donors.

GARDP supports the IACG's emphasis that efforts to leverage existing funding mechanisms must be supported by effective global, regional and national governance and coordination mechanisms to help direct resources to agreed priorities, but this must also include the use of common principles to ensure sustainable access.

Recommendation E1: If a One Health Global Leadership group on AMR supported by a constituency-based platform were to be agreed, **GARDP suggests** there are representatives from countries in the Northern and Southern hemispheres to reflect the global challenge, clear terms of reference, conflict of interest rules and transparency of process and key outcomes.

Recommendation E2: GARDP supports an independent panel on evidence for action against AMR. GARDP suggests the need for strong provisions to ensure independence and appropriate representation in order to maintain integrity, avoid overlap and ensure collaboration.

Global Antimicrobial Resistance (AMR) Research and Development (R&D) Hub

 From:
 Elmar Nimmesgern

 To:
 IACG-secretariat

 Cc:
 Global AMR R&D Hub

Subject: feedback from the Secretariat of the Global AMR R&D Hub

Date: Monday, February 18, 2019 17:17:10

Dear Sir or Madam,

I am providing feedback to the consultation on the draft recommendations of the IACG on behalf of the <u>Secretariat of the Global AMR R&D Hub</u>.

The Global Antimicrobial Resistance (AMR) Research and Development (R&D) Hub was launched in May 2018, following a call from the G20, to address challenges and improve coordination and collaboration in global AMR R&D in a One Health approach. The Global AMR R&D Hub supports global priority setting and evidence-based decision-making on allocation of resources for AMR R&D through the identification of gaps, overlaps and potential for cross-sectoral collaboration and leverage in AMR R&D. It is a global partnership of 15 countries, the European Commission and two philanthropic foundations. The Secretariat of the Global AMR R&D Hub implements the Work Plan approved by the Board of Members.

My name is Elmar Nimmesgern and I am the Secretariat Lead of the Global AMR R&D Hub.

Thank you for the opportunity to provide feedback on the Draft Recommendations. The Secretariat of the Global AMR R&D Hub focuses its feedback on the Innovate to Secure the Future and Strengthen Accountability recommendations. The Secretariat of the Global AMR R&D Hub could also support the work of the Independent Panel called for under recommendation E2 in the section with Global Governance recommendations.

Innovate to Secure the Future

The Secretariat of the Global AMR R&D Hub agrees that the recommendations provided in the Innovate to Secure the Future section should focus on increasing investment and innovation, promotion and support of equitable and affordable access, and strengthening research collaboration. Suggestions to strengthen the recommendations and to acknowledge the role the Global AMR R&D Hub will have in this space are provided below.

Recommendation B1

As noted in the considerations for the recommendations text, implementation and operational research is also required to help address AMR especially on how to effect behavioural change and improve stewardship and infection, prevention and control in all One Health sectors. The text of the recommendations currently only highlights the need for new antimicrobials, diagnostics, vaccines, waste management tools and alternatives to antimicrobials. It is suggested that the importance of implementation and operational research is also captured in the recommendations. In addition, research into improving existing interventions and technologies should not be precluded from the recommendations with the inclusion of 'new'.

Recommendation B3

The Global AMR R&D Hub was established, following the call from the G20 in 2017, with the ambition to help address what is Recommendation B3 in the IACG report. As outlined in its published workplan, the Global AMR R&D Hub has already taken steps to begin mapping global AMR R&D activities and initiate global conversations. In December 2019, the Global AMR R&D Hub will launch the first stage of its dynamic dashboard which will provide close to real time information of AMR R&D activities globally. In addition, the work plan outlines how the Hub will promote high-level coordination among governments and funders in order to better align national and international R&D efforts to address AMR. The Global AMR R&D Hub is open to all countries and important non-governmental donors. To complement the role of the Hub and to reduce potential duplication of efforts, it is proposed that the draft recommendation calls for further support and participation in the Global AMR R&D Hub to support its role in coordination and facilitating collaboration of international research efforts in AMR. In addition, member states could be encouraged to include in their National Action Plans identification of all relevant research activities at the national level and provision of AMR R&D data to the Global AMR R&D Hub.

There is also an opportunity to strengthen the recommendation (B3c) for increased collaboration between funders and researchers to also include coordination and collaboration of the various research initiatives.

Suggested text changes to Recommendation B3 are:

The IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context by:

a. Undertaking coordinated global mapping of research and development activities and funding to address antimicrobial resistance and supporting the Global Antimicrobial Resistance Research and Development Hub (Global AMR R&D Hub) in carrying out its high-level global mapping of research and development activities.

To support the proposed change in the recommendation, it is suggested that the bullet points of the consideration section be amended to:

- The IACG recognizes past and current efforts to promote and enhance research collaboration and interdisciplinary approaches to address antimicrobial resistance and to map research activities, including through JPI-AMR, the Global Antimicrobial Resistance AMR R&D Research and Development Hub and the STAR-IDAZ International Research Consortium on Animal Health, as well as in the private sector. It is recommended that the Global AMR R&D Hub enhance coordination between these collaboration initiatives. However, it emphasizes that -This will help address the lack of information, collaboration and transparency across different research and development activities, funding agencies and partners which continues to act as significant barriers to advancing research and development on antimicrobial resistance.
- The IACG notes that information sharing, collaboration and coordination of research and development through ongoing and future initiatives across all sectors will help in identifying global research and development priorities, ensure that funding addresses those priorities

along the full research and development pipeline, enable gaps to be identified and monitored, maximize the impact of research and development, and help to reduce costs and duplication of effort.

• The IACG recommends that, wherever possible, existing research and development platforms for animal and human health, and for the environment, should formalize information sharing and collaboration arrangements and that this could be supported by the Global AMR R&D Hub, as appropriate.

Strengthen Accountability and Global Governance

The Global AMR R&D Hub anticipates that it will be able to provide evidence of AMR R&D to assist the proposed Independent Panel On Evidence for Action against AMR to provide regular reports as noted in Recommendation E2.

Kind regards Elmar Nimmesgern



Dr. Elmar Nimmesgern Secretariat Lead Global AMR R&D Hub



13 February 2019

DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE (January 2019)

Feedback by

THE JOINT PROGRAMMING INITIATIVE ON ANTIMICROBIAL RESISTANCE (JPIAMR)

The JPIAMR strongly welcomes the recommendations of the IAGC and appreciates the recognition and support for the JPIAMR and its activities throughout the document.

We would like to address some specific comments regarding few of the recommendations:

Recommendation A2: The IAGC highlights the need for calls on all individual Member States to accelerate the development and implementation of One Health National Antimicrobial Resistance Action Plans within the context of the SDGs that, at a minimum, include:

c. Technical co-operation, capacity development, research and (...).

The JPIAMR Member States have aligned their national action plans on research in alignment with the JPIAMR Strategic Research Agenda and would welcome the recommendation that individual countries collaborate in research through international initiatives, such as JPIAMR, to facilitate the implementation of this action.

e. Effective national coordination, accountability and governance mechanisms.

We suggest to also include "international" as "e. Effective national and <u>international</u> coordination, accountability and governance mechanisms. "

Recommendation B1: The IAGC calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials – particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials – for human, terrestrial and aquatic animal and plant health.

• It would be very useful if this sentence reference specifically to the "One Health setting" and also to include the area of "infection, prevention and control".



Recommendation B3: The IAGC calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context by:

- a. Coordinated global mapping
- JPIAMR appreciates the acknowledgement of our previous mapping efforts in 2014 that is going to be updated by the public publication of a new investments and research projects map this February 2019 with we data from our 27 member countries.
- The JPIAMR concur with IACG analysis that transparency between funding agencies could improve and urge the IACG to recommend all the Member States to collect data of research and developmental activities and share them with international mapping exercises.
- b. Establishing and maintaining a platform for sharing information research and compounds in development
- In relation to B3 b, c, d the JPIAMR would like to highlight the development of the
 JPIAMR Virtual Research Institute (JPIAMR-VRI) as one of its key activities. The JPIAMRVRI is a One Health virtual platform to connect research networks and research
 performing organisations to conduct collaborative research on the JPIAMR Strategic
 Research Agenda priority topics.
- The JPIAMR-VRI will provide resources for knowledge exchange, increased research
 coordination and capacity, as well as support for sharing of resources, data, and
 research results. It will foster coordination, collaboration and alignment of
 antimicrobial resistance research.

Recommendation D2: The IAGC emphasizes the need for increased investment in the global response to antimicrobial resistance:

- The JPIAMR welcomes the recognition by the IACG for supporting the advancement of the global response to antimicrobial resistance.
- The JPIAMR currently has 27 member states who work together to fund research into antimicrobial resistance. In the current JPIAMR call on Diagnostics and Surveillance (2019) JPIAMR has enlisted the support of development agencies to extend the direct funding of the researcher portfolio to low and middle income countries in Asia and Africa. The further inclusion of additional Member States, and funding agencies will further enhance extend the global reach of research funding by portfolio of the JPIAMR.

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On behalf of the JPIAMR Board

Medicines for Malaria Venture

From: Silvia Ferazzi
To: IACG-secretariat
Cc: Andrea Lucard

Subject: Public discussion - Draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial

Resistance

Date: Tuesday, February 19, 2019 14:38:48

Attachments:

Dear Madam, Dear Sir,

The organization Medicines for Malaria Venture would like to commend the Ad Hoc Interagency Coordination Group on Antimicrobial Resistance for its informative report and its comprehensive attention to all forms of antimicrobial resistance throughout the document. We would like to submit the following comments to a few sections of this report:

Page 4, white bullet 2 (Effective nation-level antibiotic demand forecast): stronger demand forecast capacity in countries is indeed a very important requirement, which applies to interventions across all form of antimicrobial resistance. We would suggest replacing the word antibiotic where relevant: "Effective national-level antibiotic antimicrobial demand forecasts: Improved forecasting is needed in both human and animal health to improve access to antibiotics antimicrobials and to strengthen procurement and supply chain management. This will in turn support efforts such as those by WHO and OIE to develop a global demand forecast model for antibiotics that can be shared with manufacturers and procurement agencies on a regular basis and made publicly available".

page 7, bullet point 4 ("The IACG acknowledges ..."): several other mechanisms and partnership have been addressing crucial R&D areas in support of the fight against resistance from a variety of antimicrobial threats, such as Medicines for Malaria Venture in the area of antimalarial resistance. We would suggest this bullet point to be either more comprehensive of the role of other partnerships in the fight against antimicrobial resistance, or less specific "The IACG acknowledges the important and encouraging role of existing international mechanisms and innovative partnerships to support research and development in human health and the fight against antimicrobial resistance. It recommends full and sustained funding for such initiatives..."

Page 9, bullet point 2 ("The IACG notes that ..."). This recommendation could be more specific in referencing the importance of open data sharing in the discovery phase, based on examples such as the MMV Pathogen Box or the newly launched DNDi/MMV Pandemic Response Box, which are being used for research on drugs against multiple pathogens at risk of, or currently experiencing, resistance. The recommendation for example could read: "The IACG notes that information sharing and use of existing and new open data sharing platforms in R&D, as well as collaboration and coordination of research and development through ongoing and future initiatives across all sectors and across diseases at threat of antimicrobial resistance, will help in identifying global research and development priorities, ensure that funding addresses those priorities along the full research and development pipeline, enable gaps to be identified and monitored, maximize the impact of research and development, and help to reduce costs and

duplicat	ion of effo	rt".	
Yours fai	thfully,		
Silvia Fer	azzi		
Director, A	Advocacy		
	s for Malar g Malaria To	ia Venture ogether	MMV

Medicines Patent Pool (MPP)



Draft Recommendations of the AD Hoc Interagency Coordination Group on Antimicrobial Resistance

Medicines Patent Pool Comments

The Medicines Patent Pool (MPP) would like to welcome this additional opportunity to provide feedback on the draft recommendations of the Interagency Coordination Group on Antimicrobial Resistance (IACG).

Access for all to ensure progress

- We are very pleased to see that the first IACG recommendation to accelerate progress in the AMR response is to provide affordable access to new and existing antibiotics, drugs, diagnostic and vaccines at affordable prices for those in need of treatment. Medicines must be available and affordable for biomedical innovation to make a real contribution to global health. In a recent article, Kållberg et al have found that of the twenty-five new antibiotics introduced between 1999 and 2014 only twelve had registered sales in more than ten countries, and typically with little to no spread to LMICs¹. With new antibiotics under development being in many cases developed by small companies with limited global reach, there is a risk that this trend continues and that people in need in LMICs will not have access.
- The experience of the MPP in HIV and Hep C has provided a concrete example of how patent pooling can help ensure that new medicines become rapidly available and affordable to people needing them in low- and middle-income countries (LMICs). The MPP model has also demonstrated that it contributes to addressing the need for follow-on innovation in relation to products needed mostly in developing countries, such as new combinations of medicines that are patented by more than one entity. A prime example of implementation of the model is the development of the new fixed dose combination comprising tenofovir, lamivudine and dolutegravir ("TLD"), which is now recommended by the WHO as the preferred first line regimen for HIV treatment.

Incentives to promote innovation

• We welcome the recommendation from the IACG asking for global access initiatives like the MPP to consider access to new and existing antibiotics, which is fully aligned with what we are currently exploring. Last May, the MPP released the results of a feasibility study exploring the possibility of expanding its mandate to work on other patented essential medicines, including new antibiotics of public health priority. The feasibility study provided the technical analysis for the MPP to expand its mandate beyond HIV, TB and hepatitis C. Over the coming months, the MPP will be working on prioritizing possible candidates for in-licensing, including exploring its possible role in relation to new

¹ Cecilia Kållberg *et al*, "Introduction and Geographic Availability of New Antibiotics Approved Between 1999 and 2014," PLOS ONE, Oct. 16, 2018. Available

at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0205166



antibiotics for combatting AMR, taking into consideration the AWaRe categorization of the WHO.

- We agree that financial and non-financial incentives should be based on the principles outlined in the 2016 UN Political Declaration on Antimicrobial Resistance. These principles call for the de-linking of the financing of research and development for new antibiotics from the price and volume of sales to facilitate equitable and affordable access and to avoid perverse incentives that may lead to excessive use. The MPP can contribute to the implementation of these principles by supporting efforts to manage IP on new antibiotics in a public-health oriented manner that promotes innovation and facilitates both access and stewardship.
- We agree with the IACG that any financial or non-financial market incentive to address AMR should be aligned with R&D needs and priorities targeting to address the bottlenecks and market barriers across the product cycle. Linking prizes or other incentives offered by different innovative R&D financing mechanisms to MPP licensing could contribute to ensuring that new products become available in LMICs under provisions that consider good stewardship practices.

Incentives for manufacturers

- The demand for new antibiotics in LMICs will likely be limited and stewardship
 requirements that restrict marketing and/or distribution channels may limit further the
 market attractiveness for manufacturers, even if licences were available. It is therefore
 important for the IACG to consider whether appropriate incentives may also be needed
 to ensure that manufacturers remain interested in producing antibiotics of public health
 significance for LMICs, including those that are meant for Watch or Reserve.
- We support the request to leverage existing global pool procurement initiatives or the
 promotion of a new global procurement agency to include antibiotics. This would help
 to secure the supply of quality assured medicines, contribute to good stewardship and
 may help to enhance predictability of demand for manufactures that supply LMICs.

Collaboration among key stakeholders

• As suggested by the IACG, we welcome the request for further collaboration and information sharing between different stakeholders, including the private sector, to ensure affordable access, prudent use and stewardship of antimicrobials. The MPP is keen to work closely in collaboration with the industry and with recent mechanisms established to support R&D for new antibiotics, such as CARB-X or GARDP. CARB-X, an initiative to stimulate the early- stage pipeline for antimicrobials targeting priority pathogens, already requires its grantees to develop an access and stewardship plan for its drug candidates that advance through the pipeline and has indicated that licensing to the MPP could be one option for grantees to fulfil this requirement.



Licensing to implement stewardship clauses

As mentioned in our previous submission, the MPP is already implementing, monitoring, and enforcing certain stewardship-related obligations in its current licenses with drug manufacturers. In Tuberculosis (TB) for example, the licence signed by MPP and the Johns Hopkins University on sutezolid, includes provisions to ensure that commercialization of the product follows proper stewardship. The TB Stewardship Report, which we published in 2016, examined how MPP licences could contribute to both affordable access and responsible stewardship for new TB drug². These could be further enhanced in relation to AMR. Through its licensing agreements and careful monitoring of compliance, the MPP can ensure that there are binding obligations in a number of areas in which manufacturers would be expected to contribute to the stewardship of new antibiotics. These could include, for example, licensing provisions that ensure that products comply with quality assurance standards, that there are appropriate controls on environmental discharge from pharmaceutical manufacturing, that marketing practices are appropriate and contribute to appropriate use, or that new antibiotics are sold through appropriate channels to decrease the risk of resistance. The licences can also contribute to ensuring that people in LMICs who need them get access.

Benchmarks needed for responsible behavior

 In addition to clauses to ensure appropriate marketing of new antibiotics and those to regulate environmental discharges in manufacturing, there is a need to develop appropriate standards that can be expected from manufacturers of antibiotics in a range of other areas. We, therefore, very strongly support the IACG recommendation for the early adoption and implementation of global standards and best practices by the Tripartite+ and other international and national authorities, so that those norms and standards could be used as a benchmark for responsible behaviour from all parties.

² The Medicines Patent Pool Foundation. TB Stewardship Report. 2016. https://medicinespatentpool.org/uploads/2017/07/STEWARDSHIP-REPORT_FINAL-1.pdf

Pew Charitable Trusts



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February 18, 2019

Dr. Tedros Adhanom Ghebreyesus and Ms. Amina Mohammed **Co-Chairs**

U.N. Interagency Coordination Group on Antimicrobial Resistance (IACG)

RE: Public Discussion on the draft recommendations of the Ad hoc Interagency Coordination **Group on Antimicrobial Resistance**

Dear IACG Co-chairs,

The Pew Charitable Trusts (Pew) appreciates this opportunity to provide comments on the draft recommendations of the Ad hoc Interagency Coordination Group on Antimicrobial Resistance (IACG). Pew applies a rigorous, analytical approach to improve public policy, inform the public and stimulate civic life. Through our Antibiotic Resistance Project, we seek to reduce public health risks posed by the inappropriate use of antibiotics in humans and animals by creating incentives for the implementation of judicious use principles and practices, strengthening oversight, and fostering innovation in drug development.

Pew applauds IACG's efforts to address the important issue of antibiotic resistance that poses a threat to global health. As drafted, the proposed recommendations identify important actions that will foster antibiotic stewardship. However, Pew suggests the following additions to the current draft:

1. Highlight successful examples of multi-sectoral, public-private and private-private partnerships in the animal agricultural sector and emphasize their critical importance for fostering the implementation of antibiotic stewardship.

Meaningful progress in the fight to combat antibiotic resistance cannot be achieved without successful stakeholder collaboration. In the current draft recommendations, several sections place great emphasis on the importance of collaboration and highlight successful models, but examples from the animal agriculture space are largely missing (see for instance recommendations B1, E3). Moreover, the critical importance of such collaborations for stewardship implementation in agricultural settings should be more clearly emphasized (e.g., recommendation A1).

Pew has moderated a two-year dialogue among stakeholders in the U.S., including major food companies, retailers, and livestock, trade and professional associations, to ensure that antibiotics are used judiciously throughout production to protect animal and public health. The resulting framework, which was released on December 18, 2018, defines effective antibiotic stewardship for animal agriculture and lays out its core components and guiding principles for implementation.

The 15 core components of the antibiotic stewardship framework are based on the importance of veterinary guidance and partnership, disease prevention strategies, and optimal treatment approaches, as well as record keeping and a culture of continuous improvement and commitment to antibiotic

stewardship. The components address education, implementation, and evaluation steps for phasing in stewardship programs. The framework's guiding principles are intended to help ensure that stewardship programs have a clear scientific basis, are transparent, minimize the risk of unintended consequences, encourage alternatives to antibiotics, and focus on long-term sustainability. Ultimately, the framework seeks to foster and validate the continuous improvement of science-based and validated stewardship practices, and to implement best practices throughout the animal production system. It is one recent example of the important role industry and professional societies play in animal antibiotic stewardship implementation, and highlights the crucial importance of cross-sector collaboration.

2. Add references to relevant existing initiatives and resources to provide practical guidance for the implementation of key recommendations around antibiotic stewardship in animal agriculture

Some sections of the recommendations extensively reference existing efforts and resources (e.g., recommendation B1, C1 or D2), but others would benefit from a more comprehensive discussion of pertinent existing initiatives (e.g., Codex risk assessment process for Recommendation A3, GLASS (Global Antimicrobial Resistance Surveillance System) for Recommendation A2). Because the recommendations can provide an important roadmap for efforts to combat antibiotic resistance, their usefulness would be strengthened by the inclusion of more references to relevant existing initiatives and resources. These references would be a valuable source of information on previous efforts to address the issue identified in the recommendation, thereby providing important historical context for the recommendations as well as practical guidance for their successful implementation at the national or local level.

3. Emphasize the role of international organizations and agreements as a catalyst for countries to phase out growth promotion uses.

Pew fully supports the IACG's call to phase out growth promotion uses of antibiotics globally, and to start by immediately ending the use of critically important antibiotics for this purpose. However, the relevant section in the draft recommendations (see considerations for Recommendation A3) could be further strengthened. International organizations and agreements such as the Codex Code of Practice or the OIE Terrestrial manual can have far-reaching consequences, governing interactions among Member Countries and exerting a catalytic effect on policy priorities. This reality, in particular as it pertains to efforts to phase out growth promotion uses of critically important antibiotics globally, should be more clearly highlighted (see recommendation A3).

In conclusion, Pew commends IACG for developing these draft recommendations. They will be an important catalyst for change and help further efforts to combat antibiotic resistance.

Sincerely,

Kathy Talkington, Director Antibiotic Resistance Project The Pew Charitable Trusts Karin Hoelzer, Senior Officer Antibiotic Resistance Project The Pew Charitable Trusts



Development, Innovation and Intellectual Property Programme

RESPONSE BY SOUTH CENTRE TO THE PUBLIC DISCUSSION ON THE DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE (IACG)

The South Centre welcomes the opportunity to provide comments on the draft recommendations of the IACG ahead of the report's submission to the United Nations Secretary-General by April 2019.

Recognizing the work of the IACG, the South Centre encourages the IACG to convey the urgency of addressing antimicrobial resistance and to make bold and concrete recommendations that catalyze and accelerate global action.

We note that various elements now presented in the 'considerations' may be included in the 'recommendations' to provide more precise guidance for their implementation. Our main specific observation is that tackling antimicrobial resistance demands a concerted and effective global action, and this will require appropriate financial and technical resources to support developing countries in implementing national action plans, including investing in strengthening health systems, expanding access to clean water and sanitation, and transforming food production systems. This issue remains in our view insufficiently addressed in the draft document.

The following comments and suggestions are also put forward for consideration of the IACG:

Access

The South Centre supports the draft recommendation A1 and calls for all countries to ensure equitable and affordable access to existing and new antimicrobials. Improving access to drugs, vaccines and diagnostics is essential to tackle antimicrobial resistance (AMR), in particular in developing countries where lack of equitable access to affordable drugs, vaccines and diagnostics is a major barrier. The South Centre supports the consideration of the concrete ideas presented in the consideration section, including establishing national notifications systems for shortages and stock outs, improving demand forecasting, establishing production facilities and supporting pooled procurement.

Providing affordable access is identified as an important area for government action. However, more concrete guidance should be provided by IACG on the type of policies, measures and mechanisms that governments can establish to provide for existing and new drugs, diagnostics and

vaccines at affordable prices; including to people who are unable to pay for them. For example, the United Nations 2016 Political Declaration recognized the importance of delinking the cost of investment in R&D from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools, vaccines and other results to be gained through R&D.

The main text of the recommendation could include explicit reference to diagnostics and vaccines.

The South Centre welcomes the endorsement of the IACG to the principles contained in the United Nations 2016 Political Declaration, stating that research and development (R&D) efforts should be needs-driven, evidence-based and guided by the principles of affordability, effectiveness, efficiency and equity. The recommendation should provide, however, more specific guidance to global and national R&D initiatives to ensure that they apply these principles and for other parties to be able to monitor them for accountability. As noted above, delinkage of the cost of investment in R&D from the price and volume of sales is recognized as an important means of promoting equitable and affordable access.

Recommendation B2 to increase global initiatives to improve access, particularly to address the needs of low-income countries, is welcome.

Linkage of National Action Plans to Sustainable Development Goals

The draft recommendation A2 call to accelerate development and implementation of one health national action plans (NAPs) in the context of efforts to achieve the sustainable development goals (SDGs) is welcome. The recommendation nonetheless does not advance ideas on how the mainstreaming of AMR efforts with sustainable development and SDG progress can be fostered, in particular in the area of providing technical and financial support for low and middle income countries.

Innovation

Recommendation B1 calls to provide sustained financing to partnerships on R&D, such as CEPI, CARB-X and GARDP. It is implicit that all such partnerships will improve affordable access to health products. However, this may not be the case. For example, CEPI currently does not have a clear access policy to ensure that the products that are developed will be affordable. Any funding to support new or existing R&D initiatives should be subject to these efforts being based on the principles of affordability, effectiveness, efficiency and equity. These principles are stated in the recommendation yet no guidance is provided on how to monitor that product development partnership and other R&D initiatives implement them.

Recommendation B1 rightly stresses the importance of developing new antibiotics and this should be accompanied with increased financial support for initiatives that are looking into other needed alternatives, such as repurposing older antibiotics, exploring the role of combination products and research and development on finding new diagnostic and vaccine technologies.

Regarding the current consideration on how to address the issue of substandard and falsified medicines, more emphasis should be placed in supporting the capacity of national regulatory systems.

Civil Society engagement

The South Centre supports the increased engagement of civil society groups and consumer groups on AMR action and welcomes the recommendation C1. Increased financing to support their efforts is needed.

Financing and Monitoring

A major obstacle for developing countries to increase action on AMR is the lack of financial and technical resources. More innovative and concrete suggestions should be given by IACG on how to mobilize increased resources towards developing countries as priority.

The recommendation provides different options for mobilizing existing finance and mainstreaming AMR into other development programmes and existing international aid. While this is key in the wider response for financing, a clear case needs to be made for making new financing available to respond to the multifaceted challenges posed by AMR, such as transition funds for smallholder food producers to adopt more sustainable practices without the routine use of antibiotics The recommendations should more clearly reflect the investment areas that are needed both on national and global levels. On a national level the recommendations should call for member states to step up their domestic funding efforts for the implementation of NAPs. On a global level the recommendations should call for securing finance of the functions required for the global coordination of the response to AMR

The call for using the "AMR lens" provides a platform for broader awareness and this should rightly be applied to existing funding initiatives. Additionally, integrating monitoring and measuring of results will be needed and also directing it to where it will generate impact in tackling AMR issues. AMR will also need to be mainstreamed into broader initiatives including universal health coverage and the sustainable development goals through indicators. Likewise, key agencies working on development such as the United Nations Development Programme (UNDP) and the United Nations International Children's Emergency Fund (UNICEF) should be included in implementation efforts.

The recommendations call for an increase in the mandate of the tripartite agencies plus UNEP to provide capacity building and technical support. However, this will need to be accompanied by the means for the agencies to do so and therefore an increase of the funding available to carry the mandate to increase country level support and ensure accountability mechanisms.

Global Governance

The South Centre supports the call for an Independent Panel on Evidence for Action. The Panel should be supported with adequate resources and mechanisms to ensure that no vested interests influence its work. Furthermore, any multi-stakeholder engagement should be clear on how it will avoid conflict of interest and when not possible enacting robust guidance on how conflict will be

managed or mitigated. The proposal of a One Health Global Leadership Group for AMR would need to be more specific on how this group will be formed, where will it be located, who will be a part of it and what the reporting mechanisms would be.

The IACG should make a clearer call for its recommendations to be considered as part of the ongoing process of developing and finalizing the Global Development and Stewardship Framework (GDSF) by member states of the Tripartite agencies—the World Health Organization, the Food and Agriculture Organization and the World Organisation for Animal Health— (WHO-OIE-FAO) plus UNEP. This will help to ensure accountability and emphasize the need for policy coherence. The GDSF will become a guide on how to design access and stewardship measures that countries can apply. As such it is critical that the GDSF is designed to meet the access and stewardship needs of all member States, including developing countries.

DRAFT RECOMMENDATIONS OF THE AD HOC INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE

Feedback provided on behalf of the Stop TB Partnership by
Dr Lucica Ditiu (Executive Director)
Dr Sahu Suvanand (Deputy Executive Director)
Dr Jacob Creswell (Coordinator, Innovations and Grants Team)
Dr Viorel Soltan (Team Leader, Country and Community Support for Impact Team)
Dr Sreenivas Nair (Regional Advisor, Country and Community Support for Impact Team)
Mr James Malar (Global Fund Project Officer, Country and Community Support for Impact Team)

Dr Brenda Waning (Chief, Global Drug Facility)
Mr Brian Kaiser (Technical Officer, TB Medicines Market Strategies)
Mr Wayne Van Gemert (Technical Officer, TB Diagnostics Market Strategies)
Dr Michelle Imison (Advocacy Officer, UN High Level Meeting on TB, Advocacy &
Communications Team)

Recommendation A1: The IACG calls on all Member States to ensure equitable and affordable access to existing and new quality-assured antimicrobials and their prudent use by competent, licensed professionals across human, animal and plant health. This recommendation must be supported by efforts both to reduce the need for antimicrobials and improve access through:

- a. Lowering the prevalence of infection through clean water, sanitation and hygiene;
- b. Decreasing the likelihood of diseases and their spread through delivery of existing vaccines and strengthening infection prevention and control measures;
- c. Ensuring best practices in terrestrial and aquatic animal and plant health, food production and waste management;
- d. Supporting behaviour change through effective communication and incentives targeted at the public and professionals in human, terrestrial and aquatic animal and plant health, as well as food production and the environment;
- e. Developing national instruments based on international standards for equitable access to and prudent use of existing and new quality-assured antimicrobials in humans, animals, plants and food production, as well as waste and water management in health care, manufacturing and farming-related activities; and
- $f.\ Strengthening\ national\ surveillance,\ regulatory\ and\ accountability\ mechanisms.$
 - The Stop TB Partnership suggests that this recommendation could benefit from defining a standard that would make an antimicrobial "quality-assured" – for example WHO Prequalification or Stringent Regulatory Authority.
- There is very little reference to how to address substandard prescriptions and adherence monitoring – at least stronger regulations and strict monitoring could be included. Quality assurance of drug-testing facilities and better systems and processes for quality assurance need to be highlighted. These additions would underline the importance of addressing the root causes of AMR.
- From among the Considerations for this Recommendation:
 - Second bullet, second sub-bullet on global demand forecast: It may be helpful to focus global demand forecasting on small volume/small market products that could benefit from this approach.
 - Second bullet, third sub-bullet on establishing local production facilities: this seems counterproductive to other Recommendations in this section about global demand forecasts and pooled procurement approaches. Additionally, local production of vaccines should not be recommended in most cases.

Recommendation A3: The IACG calls on all Member States to phase out the use of antimicrobials for growth promotion, consistent with guidance from the Tripartite agencies (FAO, OIE and WHO), starting with an immediate end to the use of the Highest Priority Critically Important Antibiotic Agents (i.e. quinolones, third- and higher- generation cephalosporins, macrolides and ketolides, glycopeptides and polymyxins).

• The Stop TB Partnership suggests that 'phase out' is too weak a recommendation. This practice needs to be stopped altogether with no compromise.

Recommendation B1: The IACG calls upon public, private and philanthropic donors and other funders to increase investment and innovation in new antimicrobials - particularly antibiotics, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials - for human, terrestrial and aquatic animal and plant health through:

- a. Financial and non-financial incentives strategically targeting the most important research and development needs, scientific challenges, and market barriers based on the principles of affordability, effectiveness, efficiency and equity, as outlined in the 2016 UN Political Declaration on Antimicrobial Resistance; and
- b. Building upon existing Product Development Partnerships in human health and establishing more of them, particularly for terrestrial and aquatic animal and plant health.
- The Stop TB Partnership suggests the addition here of a reference to TB and existing TB-specific initiatives.
 - Existing TB-related PDPs (e.g. FIND, TB Alliance) are fairly mature and offer useful lessons and models for ways forward in developing similar mechanisms for AMR.
 - In addition the Political Declaration from last year's UN High-Level Meeting on TB (UNHLM on TB) contained a target to successfully treat 1.5m people with DR-TB (including 115 000 children) by 2022 – the first global target on AMR.

Recommendation B2: The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

- The Stop TB Partnership suggests that social and cultural barriers to accessing health services
 and care including human rights and gender related barriers (e.g. stigma) particularly for
 the most vulnerable populations (e.g. criminalized populations, people who use drugs or
 undocumented migrants) should be explicitly highlighted.
- This recommendation may benefit from indicating these initiatives should promote access to
 existing and new quality-assured products (assuming quality-assured was defined previously).
- Human rights are not mentioned in this document at all, and gender is only mentioned in the
 context of gender mainstreaming. There are references to these aspects in the Political
 Declaration of UNHLM on TB which could guide what was included here and it would be
 amiss for those not to be incorporated.

Recommendation B3: The IACG calls upon public, private and philanthropic research funders and other stakeholders to build upon current research and development efforts and strengthen research collaboration in a One Health context by:

- a. Undertaking coordinated global mapping of research and development activities and funding to address antimicrobial resistance;
- b. Establishing and maintaining a platform for sharing information on research and compounds in development in both ongoing and completed research and development activities;

- c. Promoting synergies and opportunities for collaboration among funders and researchers in human, animal and plant health, and the environment; and
- d. Promoting openness and transparency in data from all research and monitoring and surveillance sources.
- The Stop TB Partnership suggests that this Recommendation mention the need for R&D and innovation in relation to individual compounds but also in terms of the drug combinations needed to treat conditions (including TB).

Recommendation C1: The IACG calls for the systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels through: a. Strengthening their roles in accountability, advocacy, monitoring progress and ensuring prudent use of antimicrobials; b. Promoting synergies with consumer and civil society groups active in other sectors, including in climate change and the environment, responses to HIV, TB and malaria, Universal Health Coverage and other aspects of the SDGs; and c. Provision of political, financial and technical support for civil society organizations to enhance their engagement, including for work with governments.

The Stop TB Partnership is pleased at how well this Recommendations covers civil society. The
need to resource civil society to play the roles described could be further emphasized, since
the organizational advocacy skills and broader educational work required take time to
develop.

Recommendation C2: The IACG calls for the systematic and meaningful engagement of and enhanced action by the private sector as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels in order to ensure: a. Affordable access, prudent use and stewardship of antimicrobials; b. Ethical production, distribution and marketing practices, including through environmentally sustainable production and waste management and the elimination of inappropriate incentives to sell antimicrobials; c. Engagement by the private sector in collaborative efforts to collect, analyze and use data and realign economic incentives to improve production, distribution and marketing practices; and d. Contributions to addressing antimicrobial resistance through testing of innovative approaches, corporate social responsibility, and similar initiatives.

The Stop TB Partnership suggests that a bullet point under this Recommendation outlining
access principles for new products may be beneficial. This may include such things as voluntary
licensing of new products, such as through the Medicines Patent Pool, or removing or limiting
patent barriers altogether.

Recommendation D2: The IACG emphasizes the need for increased investment in the global response to antimicrobial resistance. It urges existing and future financing mechanisms in human, animal and plant health, as well as food production and the environment – including Gavi – the Vaccine Alliance, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Global Financing Facility, Multilateral Climate Funds, Unitaid, as well as future financing streams for Universal Health Coverage and other priority development issues, and their donors – to give antimicrobial resistance greater priority in their resource allocations. It further calls upon public, private and philanthropic donors in human, animal and plant health, as well as food production and the environment, to increase funding to contribute to addressing antimicrobial resistance, including to support implementation of National Antimicrobial Resistance Action Plans. The IACG recommends that existing and future global access initiatives should promote and support equitable and affordable access to existing and new antimicrobials, diagnostics, vaccines, waste management

tools and safe and effective alternatives to antibiotics for human, terrestrial and aquatic animal and plant health.

- The Stop TB Partnership suggests that any explicit reference (here, as well as in Recommendation B2 and elsewhere) to global access and scale-up initiatives in human health (e.g. CEPI, Gavi, Global Fund to Fight AIDS, Tuberculosis and Malaria, Medicine Patent Pool, Unitaid) also include reference to its Global Drug Facility (GDF): one of the largest supply and market-shaping mechanisms for antibiotics.
 - o In addition, GDF could have been mentioned (in Recommendation A1) among the examples of successful pooled procurement mechanisms.

Recommendation E1: The IACG recommends the urgent establishment of a One Health Global Leadership Group on Antimicrobial Resistance, supported by a Secretariat, to:

- a. Maintain urgency, public support, political momentum and visibility of the antimicrobial resistance challenge on the global agenda, and set targets;
- b. Advocate for action, including support for the expanding work of the Tripartite agencies (FAO, OIE and WHO), UN Environment (UNEP) and other international and regional entities;
- c. Monitor and report on progress, gaps and accountability in the global response to antimicrobial resistance;
- d. Expand multi-stakeholder engagement by establishing a partnership platform with the participation of Member States, UN agencies, international and intergovernmental organisations and regional entities, civil society, the private sector, researchers and other key stakeholders to develop and work towards a shared global vision and coordinated action on antimicrobial resistance;
- e. Provide advice and guidance on reports of the Independent Panel on Evidence for Action against Antimicrobial Resistance (recommendation E2);
- f. Monitor and advocate for the inclusion of antimicrobial resistance and a One Health "lens" in investments and programmes of major financing instruments for agriculture, health, development, food production and other relevant areas (recommendation D1);
- g. Identify priorities for research and development and facilitate implementation research in a One Health context; and
- h. Define the financial needs and gaps for the global response to antimicrobial resistance, including the costs of inaction and anticipated returns on investment.
- The Stop TB Partnership suggests that this leadership group should explicitly include a TB representative.

UNDP SUBMISION TO THE INTERAGENCY COORDINATION GROUP ON ANTIMICROBIAL RESISTANCE PUBLIC CONSULTATION ON THE DRAFT RECOMMENDATIONS TO THE UN SECRETARY-GENERAL

20 February 2019

The United Nations Development Program (UNDP) thanks the Ad hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance (AMR) for the opportunity to provide input into the <u>Draft Recommendations to the UN Secretary-General</u>. This submission builds on UNDP's presentation to the IACG in January 2018, the response to the April 2018 UN Foundation mapping for the Sub-Group 5 and the July 2018 submission to the IACG Discussion Paper on the Future Global Governance.

The 14 recommendations within the 5 areas of focus provide an overview of the many challenges that comprehensive and effective AMR responses need to address, at global and country levels. The complexity and multidimensionality of AMR and the One Health approach that governments have committed to requires greater coordination as well as stronger governance and multisectoral responses in the context of the 2030 Agenda for Sustainable Development (2030 Agenda) and the Sustainable Development Goals (SDGs).

Based on UNDP's experience in supporting multi-sectoral responses to HIV, health and development, UNDP would like to share the following inputs:

- UNDP welcomes the recognition that a stronger link with the 2030 Agenda and the SDGs is needed. Strengthening the linkages between AMR and the 2030 Agenda is imperative and could be done by including AMR in existing review processes, including Voluntary National Reviews (VNRs), as well as through national and global strategies and financing for SDG achievement.
- 2. UNDP welcomes the recognition of the need to support the development and implementation of global and national action plans (NAP) and strategies with a multi-sectoral One Health approach. Multi-sectoral responses should be designed to respond to the development dimensions of AMR. The recognition that AMR needs to be simultaneously addressed within universal health coverage and sustainable development strategies is also welcomed and needs to be further developed with concrete strategies to establish programmatic, governance and financing links. Strategies are also needed to support NAP implementation and to address global and national policy incoherence, insufficiently aligned governance and fragmentation.
- 3. UNDP welcomes the focus on strengthening accountability and global governance. The proposed governance structure builds on the current tripartite (WHO, FAO and OEI) partnership and expands to UNEP, and potentially other international and regional entities. AMR needs an effective multi-sectoral and multi-dimensional response and

therefore an AMR governance structure must have a "whole of UN" approach, which clear roles and responsibilities for all relevant partners.

- 4. In addition to global coordination, governance reforms should also include country strategies, for example, through the promotion of national multi-sectoral dialogue and foster whole-of-government and whole-of-society responses to AMR.
- 5. The proposal for governance reform should include an explicit strategy to facilitate increased engagement of developing countries governments and civil society. AMR is a global challenge that cuts across borders, and affects all countries, across all regions and levels of development. AMR responses should be adapted to specific country needs, context and capacities, especially those of developing countries and countries with challenging operating environments.
- 6. The response to AMR could benefit from paying more explicit and systematic attention to human rights principles, commitments and safeguards.

In conclusion, UNDP remains committed to working with the IACG, member states and other development partners in multi-sectoral responses to AMR. In line with our <u>Strategic Plan for 2018-2021</u>, UNDP could support the integration of AMR responses within sustainable development responses, including the creation of national multi-sectoral platforms and governance strategies to strengthen the inclusion and integration of environment, financing, human and animal health, food, agriculture and trade sectors, as well as other relevant partners and stakeholders including affected communities, civil society, academics, professional societies, and the private sector. UNDP has a health and development portfolio which can provide a range of important entry points and synergies for scaling up multi-sectoral AMR responses.

For more information please visit the **2018 UNDP Issue Brief on Multi-Sectoral responses to AMR**

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Wellcome Trust



IACG Public Discussion - Draft Recommendations of the Ad hoc UN Interagency Coordination Group on Antimicrobial Resistance (AMR).

Response by the Wellcome Trust - February 2019

Summary

- We commend the IACG on producing a comprehensive and ambitious set of proposals, reflecting an impressive process of engagement across sectors and continents over many months. Wellcome is glad to have been able to support this process since the establishment of the IACG in 2017.
- We encourage the IACG to now place an emphasis on engaging with the global community particularly Member States to build the case for the adoption and implementation of key recommendations.
- We look forward to further discussions over the coming months as the IACG process concludes.

Recommendations

A - Accelerate Progress in Countries

Member State action is critical to tackling AMR. Wellcome supports calls for Member States to develop and implement National Action Plans (NAPs) which embody a true 'one health' approach, and we endorse the emphasis placed by the IACG on ensuring access to safe, quality assured antimicrobials as being central to these plans. We similarly support the call to phase out the use of antimicrobials for growth promotion in animals, although recognise that the technical challenges associated with the refinement and implementation of this recommendation will require further discussion.

Wellcome believes that low- and middle-income countries face particularly acute challenges in the development and implementation of NAPs, which should be clearly highlighted by the IACG. The IACG should consider how its recommendations could lead to a step change in supporting countries to develop and implement NAPs. Linking recommendations A1 and A2 with recommendations D2 and E3 is essential if we are to see significant increase in the implementation of high quality NAPs. Development of a plan is a first step, but without strong political and financial support from Member States and across the UN System, then many of these plans will remain on paper rather than achieving full implementation.

As one approach to achieving this, Member States should be encouraged, in the considerations for recommendation A2, to develop forums for sharing their experience of developing and implementing One Health NAPs, through regional networks/bodies. Such networks could avoid the duplication of efforts and strengthen capacity.

We welcome the IACG's focus on the challenges in ensuring effective, affordable access to quality-assured antibiotics. It should be recognised that gaps in the availability of antibiotics can affect countries at all income levels, and that mechanisms to address such issues should include both country- and regional-level interventions, and engage civil society, philanthropic organisations, and the private sector. Efforts to improve access to antibiotics should be considered as essential elements of steps to support innovation in new products described in Section B of the recommendations.

B - Innovate to Secure the Future

We commend the emphasis placed by the IACG on the need to support innovative new products to tackle drug-resistant infections, particularly antibiotics. We endorse the Group's call for efforts to sustain private sector engagement and investment in this space, and the imperative to develop financial and non-financial incentives to support new product development and address market barriers to ensure new products reach the people and animals that need them.

However, we feel these recommendations could be strengthened by the IACG issuing a call to Member States to act with greater urgency in addressing the challenges of innovation in this space: failure to progress the development of new incentive models for the development of new products (antibiotics in particular) over the short term could leave to an irretrievable loss of innovation capacity and expertise. Reflecting current initiatives in the UK and Sweden, the IACG should call upon Member States to explore pilots of new reimbursement models to stimulate the development of antimicrobials, vaccines and diagnostics whilst supporting improved stewardship and access.

Wellcome fully supports calls for developing platforms to enable transparency and open access to data, having invested in initiatives to achieve such aims. Examples which could be sited by the IACG as platforms to be built on in recommendation B3 are:

- **SEDRIC**, an international think-thank of experts working together to accelerate filling the critical evidence gaps and improving translation of the evidence base into effective policy and practice interventions.
- The AMR Research Initiative, a project gathering and openly publishing data generated by industry sponsored surveillance programmes.
- The Shared Platform for Antibiotic Research and Knowledge (SPARK), a publicly available, interactive tool providing data to help scientists around the world identify urgently needed new antibiotics.
- **ClinicalStudyDataRequest.com (CSDR)**, a data sharing initiative involving academic research funders and pharmaceutical companies to list and share clinical trial datasets.

C - Collaborate for More Effective Action

As part of a strong global response to AMR, it is essential that mechanisms are found to engage all relevant stakeholders, and as such the implementation of recommendations C1 and C2 are essential. We endorse the recognition of the role that can be played by the private sector, subject to concerns about conflicts of interest being appropriately addressed.

Many civil society groups have a role in extending access and promoting effective stewardship, particularly Civil Society Organisations (CSOs) working within a country to deliver healthcare. These organisations may have unique insights in to what works in specific country contexts. Therefore, recommendation C1 could be strengthened by highlighting the role of civil society in extending access while also promoting effective stewardship.

D - Invest for a Sustainable Response

Wellcome fully supports steps taken with these recommendations to increase the engagement of financing and development institutions in efforts to address AMR. There are examples where financing and development stakeholders have had a positive impact on the approach taken to AMR, and the development of such initiatives should be supported and promoted.

E - Strengthen Accountability and Global Governance

Wellcome fully supports the recommendations to strengthen global governance, with the model of a small One Health Global Leadership group, supported by the establishment of a partnership platform which will provide a mechanism for multi-stakeholder engagement.

Similarly, we support the principle (set out in E2) of the role which might be played by a new Independent Panel to provide authoritative evidence to guide decision-making by Member States and international organisations, and to guide both the emergence of drug resistance and progress in the global response. However, we suggest that **the IACG should consider providing greater clarity on the possible operating model for both the Global Leadership group and Independent Panel, and in particular how they might interact with Member States.**

Wellcome considers implementation of this recommendation to be fundamental to the delivery of the other recommendations within the report. There have been steps (with limited success) to undertake, develop and/or implement variations of the recommendations contained within sections A to D previously. The ideas contained within recommendations E1 and E2 have yet to be tried but have the potential to provide the framework and accountability needed to ensure progress and implementation of this whole report.

The examples given in the recommendations points to the practicality and effectiveness of such structures. As recognised in the recommendations, AMR is a complex, multisectoral issue with a diverse range of stakeholders. It is difficult to see how the coordination needed to address this very serious threat can be achieved without a formal coordination group who has the authority to hold the different sectors/stakeholders to account.

Wellcome Trust would therefore suggest giving greater prominence to these recommendations within the report and request that the IACG calls on the UN Secretary General to prioritise implementation of the recommendations within this section. We would encourage the IACG to focus upon engaging member states closely in the discussion of the implementation of this section of the recommendations.

Wellcome is the UK's largest charitable foundation. Over the next five years, we plan to invest up to £5 billion in biomedical research and the medical humanities in the UK and internationally. We also support the development of new commercial innovations to improve health.

World Farmers Organisation



World Farmers Organisation, WFO Contribution to the Draft Recommendations of the Ad Hoc InterAgency Coordination Group on Antimicrobial Resistance

The World Farmers Organisation, WFO, expresses its appreciation to the FAO, the WHO and the OIE for the comprehensive draft recommendations prepared for submission to the United Nations Secretary General.

The WFO reminds that it actively participated in the High-level Meeting on Anti-Microbial Resistance held in New York, in 2016, and that the AMR issues remain high on the political agenda of the Organization. By addressing AMR issues, in fact, farmers increase the possibility to make their farms more productive and sustainable, thus contributing to combat global food insecurity and nutrition challenges. Therefore, WFO welcomes very much the opportunity of providing feedback to the draft recommendations.

Below are some considerations from WFO Farmers on the draft recommendations text:

Guiding principles:

WFO welcomes the One Health approach applied to the recommendations as the basis for strengthening existing systems and gain across the SDGs. The use of best practices as a starting point to address major challenges is also very welcome as an opportunity for the farmers to start from their success stories on AMR in both Livestock and Crop sectors and build on those to improve farmers' capacity to address AMR challenges. Moreover, WFO warmly welcomes the principle of mobilization of actions from stakeholders and strongly recommends to include the category of farmers, within those groups that have been identified in paragraph 2, page 3.

Recommendations A1, A2 and A3

WFO considers of the utmost importance to include the Farmers, through their Organizations, to be involved in the definition, implementation, monitoring and evaluation of national standards and policies to address the AMR issues in Livestock and Crop production. Famers have to be likewise included in trainings to improve the quality of farm production by improving the management of soils, water, health facilities, fertilizers and pharmaceuticals at farm levels, especially, but not only, in the case of phasing out Highest Priority Critically

Important Antibiotic Agents. The capacity of farmer-to-farmer knowledge sharing should be considered in South-South and Triangular cooperation initiatives. As far as surveillance and monitoring systems concerned (paragraph 1, page 6), WFO would like to underline the importance of involving farmers, through their organizations, not only in the development of core indicators, but also in accessing relevant aggregated data, to tackle AMR from the farmers' perspective.

Recommendations B1, B2 and B3

Research and innovation is a priority for the farmers and WFO welcomes the recommendations on improving investments in that sector. Especially considering the importance of reducing the gap between farmers and research, WFO warns the IACG to include farmers in the recommendations as key player in the diagnostics and in the development of effective alternatives to antimicrobials.

From the farmers' perspective, special attention should be devoted to the implementation and operational research, which would foster a positive transformation of the sector, including behavior change, communication, and infection prevention, prudent use of antimicrobials and effective soil, water and waste management (paragraph 3, page 8),

With regards to existing platforms for animal and human health, and for the environment, it is vital to involve farmers in the information sharing and collaboration (Paragraph 3, Page 9).

Recommendations C1 and C2

Civil Society and Private Sector have been identified as the two stakeholders to engage with in addressing the One Health response to antimicrobial resistance. However, because farmers are those who produce food and are crucial player in the crop and livestock sectors, WFO requests to include farmers as a third category of stakeholders to engage with, for a more effective global action on AMR.

Recommendations D1 and D2

WFO considers a critical element to include in the recommendations a specific reference to direct funding mechanism for the farmers to improve their capacity to address AMR issues at farm level, being it crop farming or livestock farming in all countries.

Recommendations E1, E2, E3 and E4

WFO welcomes the idea of establishing a mechanism of Governance for the implementation of the recommendations on AMR, led by relevant UN Agencies other Organizations and ask for the inclusion of the Farmers in that mechanism, namely the One Health Global Leadership Group on Antimicrobial Resistance. Likewise, Farmers should be consulted prior to the finalization of the *Global Development and Stewardship Framework to Combat Antimicrobial Resistance* so that they can contribute their experience and knowledge. For the next instruments that will be put in place by Governments alone or through multilateral institutions, WFO request that farmers are engaged at all stages, from the design to implementation to monitoring and evaluation of those instruments.

General considerations from the WFO farmers on the draft recommendations:

The global community is in urgent need of changed behavior concerning the use of antibiotics.

Perhaps the recommendations could include deadlines for the actions to be taken.

Very important factors for change from the agricultural point of view are:

- -Antibiotics should be used only after a diagnose from veterinarians, physicians or other relevant professionals.
- -These professionals, including physicians, pharmacists, veterinarians, nurses, paramedic, and community health workers, and other specialists and or paraprofessionals of the animal and plant health should preferably earn their money from advisory services and not from the selling of antibiotics.
- Farmers, as a unique sector of food producers, are those who directly implement practices that involve the use of antimicrobials in plant and animal health, therefore, they should be included in initiatives that are implemented at country level, that foresee capacity building programmes, training, education and awareness raising on AMR issues. Farmers want to collaborate with Government to increase the national production level of healthy food, they want to be considered in choices that affect the agricultural sector, to be able to contribute to the global demand of increasing healthy and nutritious production, while addressing environmental issues.