Do we need a PDP to help us deal with Antimicrobial Resistance?

How a product development partnership could promote innovation and responsible access to new antibiotics
Vision

- Establish a product development partnership (PDP) which, in collaboration with public and private partners in high-, middle and low-income countries, sustainably promotes the research and development of new antibiotics and ensures their rational use and their preservation globally
A PPP/PDP model enables to:

- establish TPPs addressing global needs
- provide a coordinated strategic approach to drug development
- engage into and stimulate pioneering long term scientific strategies
- promote new innovative incentives and ensure accountable use of funds
- Insure responsible use of and access to drugs
The model

Virtual and not-for-profit

- A “virtual” model is favored because:
  - it provides flexibility
  - does not immobilize capital and avoids costly overheads
  - facilitates collaborations with external public and private entities

- A not-for-profit model is preferred because:
  - Need assessments, TPPs definitions and scientific strategies will be defined solely by patient’s needs
  - No internal conflict to implement rationale use: no expectations of returns
  - Advocacy, fundraising and access to public funds facilitated, because no perceived or actual conflicts of interest
  - More freedom to design appropriate incentives and rewards, and to negotiate adequate premiums on the antimicrobials developed to insure patient access
Major tasks envisaged

- **Module 1: R&D**
  - Establish research priorities (i.e TPPs), focusing on upstream discovery (long term) and specific downstream projects (short term)
  - Foster “test-and-treat” paradigm by embedding point of care, fast diagnostics within the R&D strategy

- **Module 2: Economic frameworks**
  - Business models, IP strategies, reward schemes

- **Module 3: Procurement and Supply**
  - Address access strategies managing rational -but wide- use of the products from global health perspectives
Governance structure

- Should include HICs and LMICs, IOs, NGOs/not-for-profit, industry.
- Board of Director (BoD) and Scientific Advisory Committee (SAC): risk management and key strategic directions, delegate operations to Executive Team.
- BoD composition: balanced country representatives, donors, leading health and research institutions, academia, industry, « AMR-specific » NGOs,…
- Executive team: implement BoD strategy, supervise research consortiums and projects, BD activities, reward schemes and incentives, fundraising, advocacy & communication, drug facility to manage end products.
- Executive team composition: good mix of academia / not-for-profit, pharma, as well as scientific, public health and operational backgrounds.
- SAC composition: academic and private sector representation, to focus on technical issues, to provide recommendations to the Board to validate the strategy.
Sustained, significant and long term government funding key for perennial successful operations: “Antibiotic Fund”

Look additionally at new sources of funding, including from MIC

Innovative financing mechanisms (e.g. airlines levies, IFFIIm, GHIF, etc.)

...
Next steps

- Meeting report
- Side discussion at WHO EB
- Garner support at WHA via the GAP
- G7 concept note
- Coalition of countries to finance initial work
- Formal feasibility project team setup and hosting of the initial activities
Discussion points

- This is a global health agenda
- Despite several NCEs in development, identification of new anti-infective classes or new strategies to deal with infection remains a challenge => need significant governement support for basic research in anti-infectives
- Landscaping and prioritization of needs and gaps, with a forward and proactive approach in R&D in view of long timelines
- Need of mobilization of significant new financial resources: « antibiotic fund »
- Ability to construct alternative forms of incentives that promote R&D, rational use and strong implication of the private sector (eg. CEWG report, delinkage concept and beyond..)
Possible sources of finance

Fostering the development and rational use of new antibiotics: how a product development partnership could promote innovation and responsible access to new antibiotics

Technical consultation jointly hosted by the Drugs for Neglected Diseases initiative and the World Health Organization
8 - 9 December 2014

John-Arne Røttingen
Norwegian Institute of Public Health
University of Oslo
Harvard University
The Bank!

tbc
A «bath tub problem»
A «bath tub problem»

Global governance failure
  Classic collective action problem

Global market failure
  Underprovision, overprovision and insufficient innovation
Interconnectedness

Global Public Goods (GPGs)

Innovation of Antimicrobials

Solidarity

Universal Access of Antimicrobials

Appropriate Use of Antimicrobials

Externalities (regulation)
Global policy options

Global Public Goods (GPGs)

Partnership based innovation models

Capacity building and Access

Managed markets and utilization

Solidarity

Externalities (regulation)
Less Ambitious Global policy options

Global Public Goods (GPGs)

Guidelines, Standards and Norms

Solidarity

Technical support

Surveillance and Response System

Externalities (regulation)
**Goal:** the development of effective, safe, quality, suitable and affordable health technologies that existing market mechanisms & public policies fail to deliver

**Seven Core Principles**

1. **Health needs-driven** R&D
2. **Shared public responsibility** for ensuring innovation and access through sustained public investments in transformative R&D
3. **Affordability** through de-linkage
4. **Effectiveness:** health impact through innovative technologies
5. **Evidence-based** decision-making
6. **Efficiency:** improved coordination, knowledge-sharing, and value for money

**Governance and accountability**

- Multi-stakeholder engagement (government, private, and non-profit sectors) with appropriate management of conflicts of interest
- Open access to information via transparency policies
- Oversight & monitoring through regular reporting, evaluations & complaint mechanism

**Implementation Vehicle Options:**

Global framework through e.g. R&D Convention, or other (non-)legally (non-)binding instruments

**Member States**

- Contributions from non-state sources: foundations, NGOs, multilaterals, etc
- Voluntary vs Obligatory
- Mobilize financial resources
- Pooled Funding

**Global level**

- **FUNCTIONS at global/national/regional levels**
  - Monitoring
    - Generating evidence to inform decision-making via national and global Observatories for Health R&D
    - Accountability for the effective overall functioning of the system (including facilitating regulatory assessments)
  - Coordination
    - Prioritizing R&D needs
    - Enhance synergies and efficiencies via knowledge-sharing, network-building, and collaboration
  - Financing
    - Funding and stimulate priority R&D via push & pull mechanisms
    - Strengthen health R&D capacities

**Potential forms (following function):**

- Re-/Transform existing organization(s)
  - WHO Secretariat
  - TDR
  - UNITAID
  - others
- Create new organization(s)
  - GFATM model
  - TDR-like model
  - IARC-/CGIAR-models
  - CERN-/EMBL-models
  - others
Private investments

Service agreements

Licenses

Public bonds

Countries

Intl. taxation

Voluntary

Private agreement

Philanthropy

AB tax
Financing options

- **Donations**
  - Countries
    - Mandated assessed contributions
    - Voluntary contributions based on a soft norm
    - Voluntary discretionary contributions
  - International taxation
    - FTT, airline etc
    - AB consumption
  - Innovative financing
  - Philanthropic

- **Investments**
  - Public, e.g. bonds
  - Private
    - For profit model

- **Payments**
  - Members vs. non-members
    - Service agreements
    - Licenses
    - Products
Funding from governments (1)

- Mandated assessed contributions
- Mandated assessed minimum contributions and additional voluntary contributions
- Voluntary contributions based on a soft norm
- Voluntary multi-year contributions
- Voluntary discretionary contributions
Funding from governments (2)

• Criteria based voluntary financing
  – Inclusion criteria
    • HICs
    • HICs and UMICs
  – Level
    • Proportion of GDP
    • UN assessment scale
    • Proportion of GDP adjusted for GDP per capita
Financing of Demonstration Projects

• The first four demonstration projects resulting from the CEWG follow up resolutions require an investment of USD 60 million.

• The CEWG report recommended that countries should contribute proportionally to GDP when it comes to financing health R&D for the specific needs of developing countries.

• Broad mobilization of funding including from non-traditional donors is one of the potential successes which the demonstration project process should be able to demonstrate.

• The following slides describe how different groups of countries could contribute if the CEWG norm of proportional contribution is to be utilized.
1. Proportional Financing By World Bank income groups

In this slide, GDP is aggregated to World Bank income groups. Then each groups’ percentage of total GDP is calculated (left). This percentage is then applied to USD 60m to determine a proportional financing responsibility for each of the income groups (over).

2. Proportional Financing By WHO regions

Millions of US dollars to be paid for R&D, by WHO region

<table>
<thead>
<tr>
<th>Region</th>
<th>USD millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Region</td>
<td>1.23</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td>2.80</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>2.80</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>15.27</td>
</tr>
<tr>
<td>European Region</td>
<td>18.25</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td>19.64</td>
</tr>
</tbody>
</table>

Notes: Based on GDP in 2012. Data retrieved from WHO: http://apps.who.int/nha/database/Select/Indicators/en

In this slide, GDP is aggregated to WHO region. Then each region’s percentage of total GDP is calculated (left). This percentage is then applied to USD 60m to determine a proportional financing responsibility for each of the regions (over).
3. Dividing the costs between USA, Europe, BRICS and the rest of the world

In this slide, GDP is aggregated to four groups: BRICS, Europe, USA and the rest of the world. Then each groups’ percentage of total GDP is calculated (below). This percentage is then applied to USD 60m to determine a proportional financing responsibility for each of the groups (left).

Notes: Based on GDP in 2012. Data on European Region retrieved from WHO: [http://apps.who.int/nha/database/Select/Indicators/en](http://apps.who.int/nha/database/Select/Indicators/en)
Funding from governments (3)

- Pragmatic/discretionary voluntary financing
  - Political opportunities
    - PCAST – USA
    - O’Neill review – UK
    - Könberg report – Nordic countries
    - More….
  - Coalition of engaged countries
  - G7 and G20
- Move it out of the ODA/DAH discourse
  - Responsibility of MoHs
Funding sources – first steps (1)

• Establish the economic benefits of investments
  – First O’Neill report
  – World Bank study?

• Establish funding needs
  – Seed funding
    • $3 mill?
  – Start up needs
    • $100 million?
  – Longer term annual funding needs/goals?
    • 10-20% of current HIC market = around $1.5-3 billion
Funding sources – first steps (2)

• Establish a coalition of engaged countries and actors
  – > 3 HICs
  – > 2 MICs
  – > 1 LIC
  – NGOs and/or foundations

• Utilize EB and WHA in 2015
Addressing AMR: Innovation and best practices for infection control, use of medicines and technology development

Dr Marie-Paule Kieny, ADG

WHO & DNDi Technical Consultation
8-9 December, 2014, Geneva
An international response is required

- World Health Assembly May 2014 requests WHO
  - ... To develop a draft global action plan to combat AMR ... to ensure that all countries ... have the capacity to combat AMR.

- The Draft Global Action Plan to be submitted to the WHA in 2015
  - ... To apply a multisectoral approach to inform the drafting of the global action plan, by consulting Member States as well as other relevant stakeholders.... FAO, OIE.....
Guiding Principles for the Global Action Plan (GAP)

- Whole-of-society engagement
- Actions based on best available knowledge and evidence
- Prevention first
- Access not excess
- Sustainability – more likely when integrated into health systems or practices in other sectors (animal, agriculture)
- Incremental targets for implementation that recognise the different priorities and capacities of Member States
GAP has 5 strategic objectives

1. Improve awareness and understanding of AMR through effective communication, education and training
2. Strengthen the knowledge and evidence base through research and surveillance
3. Reduce the incidence of infection through effective hygiene and infection prevention measures
4. Optimize use of antimicrobial medicines in human and animal health
5. Develop the business case for investment in new medicines, diagnostic tools, vaccines and interventions
Use of medicines
Variability in antibiotic consumption in Europe 2011

Total antibiotic use in 2011, expressed in number of DDD per 1000 inhabitants per day in 12 European countries and Kosovo as compared to 29 ESAC-Net countries.

Source: WHO-EURO and ESAC-Net
Some issues identified

• Variability in levels of use: range 15.3 - 42.3 DDD/1000/day
  – Turkey highest – has stimulated interventions towards rational use
  – Armenia lowest – underuse may be related to poor availability
  – High levels of outpatient injectable antimicrobials in some countries

• Lack of information systems: rely on sales data; however will include antibiotics procured without a prescription

• Self-medication common: >50% sold OTC in most countries in spite of antibiotics being prescription drugs

• Choices vary:
  1. underuse of first line treatments;
  2. overuse of combination amoxicillin+β-lactamase inhibitors and respiratory quinolones, high use of amphenicols - some countries (chloramphenicol had been widely used for diarrhoea treatment)
How do we achieve better use of antibiotics?

– Need political commitment, intersectoral involvement & coordination (e.g. human health, animal health, agriculture)
– Availability of reliable data on use, of policy guidance and best practices
– Action at different levels – from national policies to facility level coordinated interventions
– Build and strengthen partnerships:
  a) Ministries of Health & Agriculture (human and veterinary sectors)
  b) Other countries and regional networks
  c) International agencies
  d) Organisations & institutions involved in promoting rational use
  e) Civil Society and patient organizations
  f) Others
Quality of antimicrobial agents: challenges and actions to address them

- Substandard and counterfeit antimicrobials
  - E.g. in 2014, reports of “fake” artemether & lumefantrine in combination (Coartem) without active ingredient

- Public health responses and interventions
  - Strengthen medicines regulatory authorities (MRAs)
  - Enforce regulations relating to registration, production, and distribution; enhance national laboratory capacity for quality control and monitoring; enhance capacity for inspection of manufacturing facilities
  - Eliminate irrational antibiotic combinations and irrational pack sizes; regulate the pharmacy and drug sellers to only sell antibiotics with prescription; regulate veterinary market (no antibiotics as growth promoters, separate types of antibiotics to be used in human and veterinary medicine)
  - Organize campaigns aimed at the public at large to reduce use of antibiotics
Development of new antimicrobials
Discovery of new classes of antibacterial drugs (1930s to 2000s)

In recent decades, only 2 new classes of antibiotics have come to market, and there is a dearth of novel antibiotics in the pipeline.

Need for development of therapies that do not drive resistance!

* Penicillins were the first beta-lactams. This class includes cephalosporins and carbapenems, developed in the 1960s and 1980s, respectively.

Source: Reproduced with data from 179. Modified with permission from Thomson Reuters (Professional) Ltd

Current Situation

EU, US or other investors
$300M/project

IMI

Bioventures, R&D companies
(generate IP)

Company A

sub-license to
Agrobusiness
Subsidiary Y

Market

Irrational use of antibiotics
market fall off in few years with resistance

ANTIBIOTIC X
Proposed Initiative: Innovation for AMR

Innovation

Development

Registration &
Production

Academics
Biotechs

R&D Pharma

Companies

Antibiotic
X, Y, Z...

Managed
Market

e.g. prizes, grants

R&D & generic
manufacturers

Initiative
Consortium
PDP

IP

Approx $2-5B
Towards a new initiative in support of the development and rational use of new antibiotics

WHO & DNDi Technical consultation, 8 - 9 Dec 2014, Geneva

Vision: Establish a product development partnership which, in collaboration with public and private partners in high-, middle and low-income countries, researches and develops new antibiotics and ensures their rational use and their preservation globally.

Participants: WHO, governments, academia, civil society, industry…

Expected result:
- draft concept for a PDP on antibiotics
- draft Mission statement
- roadmap for setting up, fundraising and convincing partners & donors