



World Conference on Access to Medical Products: Achieving the SDGs 2030

19-21 November, 2019 | New Delhi, India

POSITION PAPER





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Access to medicines is a critical factor for success of the 2030 Sustainable Development Goals (SDGs) that aims to ensure healthy lives and promote well-being of all people of all ages. Assuring access to medical products is key to advancing Universal Health Coverage (UHC). The main objective of the Conference is accelerating access to medical products for achieving universal health coverage in the context of SDGs.

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Abbreviations

ACRE	Advisory Committee on Releases to the Environment
ADR	Adverse Drugs Reaction
AEFI	Adverse Event Following Immunization
AICs	Atal Incubation Centres
AIM	Atal Innovation Mission
AMR	Anti-Microbial Resistance
AMTZ	Andhra Med Tech Zone
APEC	Asia-Pacific Economic Cooperation
API	Active Pharmaceutical Ingredient
ARV	Anti-Retrovirals
ATL	Atal Tinkering Labs
ATMP	Advanced Therapy Medicinal Product
AUC	African Union Commission
AUC	African Union Commission
AVAREF	African Vaccine Regulatory Forum
BARDA	Biomedical Advanced Research and Development Authority
BIRAC	Biotechnology Industry Research Assistance Council
BIS	Bureau of Indian Standards
BMGF	Bill & Melinda Gates Foundation
CARB-X	Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator
CBER	Center for Biologics Evaluation and Research
CDRH	Centre for Devices and Radiological Health, USFDA
CDSCO	Central Drugs Standard Control Organisation
CEWG	Consultative Expert Working Group
CHIMS	Controlled Human Infection Model Studies
CL	Compulsory Licensing
CSIR	Council for Scientific and Industrial Research
CTSA	Clinical and Translational Science Award
DAA	Direct Acting Antivirals
DBT	Department of Biotechnology, Government of India
DCVRN	Developing Countries Vaccine Regulatory Network
DFID	United Kingdom's Department for International Development
DHR	Department of Health Research, Government of India
DNDi	Drugs for Neglected Diseases Initiative
DPCO	Drugs (Prices Control) Order
EAC	East African Community
EDL	Essential Diagnostics List
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations

EIDs	Emerging Infectious Diseases
EMA	European Medicines Agency
FAO	Food and Agriculture Organization
FTA	Free Trade Agreements
GAP	Global Action Plan
GARDP	Global Antibiotic Research and Development Partnership
GCP	Good Clinical Practice
GMP	Good Manufacturing Practices
GPW13	The WHO Thirteenth General Programme of Work 2019-2023
HER	Electronic Health Records
HSA	Health Sciences Authority, Singapore
HTA	Health Technology Assessment
IACG	Interagency Coordination Group
ICDRA	International Conference of Drug Regulatory Authorities
ICGEB	International Centre for Genetic Engineering and Biotechnology
ICH	International Conference on Harmonization
ICMR	Indian Council of Medical Research
ICSR	Individual Case Safety Reports
IMI	Innovative Medicines Initiative
IMPRINT	IMPacting Research Innovation and Technology
IPR	Intellectual Property Rights
ISP	Information sharing platform
IVDs	In-vitro diagnostics
IVIRC	India Volunteer Research Infection Consortium
KIHT	Kalam Institute of Health Technology
LMICs	Low- and middle-income countries
MDG	Millennium Development Goals
MDIC	Medical Device Innovation Consortium
MDR	Medical Device Rules 2017
MERA	Malaria Elimination Research Alliance
MHRA	Medicines and Healthcare Products Regulatory Agency
MMV	Medicines for Malaria Venture
MPP	Medicine Patent Pool
MRCT	Multi-Regional Clinical Trials
MSF	Médecins Sans Frontières
MSME	Micro, Small and Medium Enterprises
MTAB	Medical Technology Assessment Board
NACO	National AIDS Control Organization
NCATS	National Center for Advancing Translational Sciences
NEDL	National Essential Diagnostics List
NEPAD	New Partnership for Africa's Development
NHM	National Health Mission

NHSRC	National Health Systems Resource Centre
NIB	National Institute of Biologicals
NIH	National Institutes of Health
NIMP	Non-Investigational Medicinal Product
NITI Aayog	National Institution for Transforming India Aayog
NPPA	National Pharmaceutical Pricing Authority
NRAs	National Regulatory Authorities
NTP	National TB Programme
OTC	Over-the-Counter
PAHO	Pan-American Health Organization
PANDRH	Pan American Network for Drug Regulatory Harmonization
PAP	Pan African Parliament
PDPs	Product Development Partnerships
PMDA	Pharmaceuticals and Medical Devices Agency, Japan
PMJAY	Pradhan Mantri Jan Aarogya Yojana
PPP	Public-Private Partnership
PSUR	Periodic Safety Update Reports
PV	Pharmacovigilance
REC	Research Ethics Committee
REP	Regulatory Exchange Platform
REP	Regulatory Exchange Platform
RMPs	Risk Management Plans
SAV	Safety and Vigilance
SDGs	Sustainable Development Goals
SEARN	South-East Asia Regulatory Network
SIB	School of International Biodesign
SIIP	Social Innovation Immersion Programme
STI	Sexually Transmitted Infections
THSTI	Translational Health Science and Technology Institute
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UHC	Universal Health Coverage
UMC	Uppsala Monitoring Centre
UNGA	United Nations General Assembly
UNICEF	United Nations International Children's Emergency Fund
USFDA	United States Food and Drug Administration
VL	Voluntary Licensing
WHA	World Health Assembly
WHIG	WHO Health Innovation Group
WHO	World Health Organization
WHO/PQP	WHO Prequalification of Medicines Program
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

I. Introduction

United Nations resolution titled “Global health and foreign policy” on universal health coverage adopted on 12 December 2012, urged governments to move towards providing all people with access to affordable, quality health-care services¹. On 25 September 2015, the United Nations General Assembly adopted the resolution 2030 Agenda for Sustainable Development and 17 SDGs as a universal and transformative development strategy². The 2030 Agenda commits the global community to “achieving sustainable development in its three dimensions—economic, social and environmental—in a balanced and integrated manner”.

Health is an important cross-cutting policy issue in the international agenda, as it is a precondition and an outcome and indicator of all three dimensions of sustainable development. Healthy lives and well-being for all at all ages cannot be achieved without the full commitment of governments, and participation of all stakeholders, including civil society, the private sector, academia, and other international, national, and local institutions, that influence health and wellbeing³. The Political Declaration of the High-level Meeting on Universal Health Coverage The health goals in the SDGs build on the unfinished business of the MDG era (such as on HIV, tuberculosis and malaria) and adds new targets, such as non-communicable diseases, Universal Health Coverage (UHC). “Universal Health Coverage: Moving Together to Build a Healthier World”, reaffirmed that health is a precondition for and an outcome and indicator of all three dimensions of sustainable development and the implementation of the 2030 Agenda for Sustainable Development⁴.

Following the September 2019 Political Declaration on UHC during the United Nations General Assembly (UNGA), the 2019 World Conference seeks to take forward the international and national agendas on UHC for access to medical products⁵. The Ministry of Health & Family Welfare with the support of World Health Organisation is organising the “2019 World Conference on Access to Medical Products- achieving the SDGs 2030”. The Conference is also partnered with Indian Council of Medical Research, Ministry of Health and Family Welfare, Biotechnology Industry Research



¹Resolution adopted by the General Assembly on 12 December 2012, A/RES/67/81

²Resolution adopted by the General Assembly on 25 September 2015 [without reference to a Main Committee (A/70/L.1)] 70/1.

“Transforming our world: the 2030 Agenda for Sustainable Development”

³Towards a Global Action Plan for Healthy Lives and Well-Being for All, Uniting to accelerate progress towards the health-related SDGs, WHO/DCO/2018.3 © World Health Organization 2018

⁴<https://www.un.org/pga/73/wp-content/uploads/sites/53/2019/05/UHC-Political-Declaration-zero-draft.pdf>

⁵That include medicines, vaccines, diagnostics, devices.

Assistance Council (BIRAC), a public sector undertaking of the Department of Biotechnology, and Translational Health Science and Technology Institute (THSTI), an autonomous institute of the Department of Biotechnology, Ministry of Science and Technology, Government of India.

The 2019 World Conference is a follow on from two previous World Conferences held in New Delhi where all stakeholders get together for renewing commitment for purposeful outcomes for attaining the global goals⁶.

Access to medical products and creating an enabling legal and trade environment for public health are critical to achieving the SDGs2030 Agenda. In a fast changing world, these issues require continuous engagement and dialogue. The 2019 World Conference will take forward the international and national discussions for access to medical products on themes organized in plenary and parallel sessions covering:

- UHC and innovation,
- regulation of medical products and access,
- legal landscape and trade-related aspects in the context of access to medical products.

The main objective of the 2019 World Conference is to make for access to medical products for achieving universal health coverage in the context of SDGs.

⁶The documents and reports of the two previous World Conferences held in New Delhi may be accessed at <http://www.worldsdg2030.org/reports.aspx>.

II. The Sustainable Development Goals (SDGs)

In the 2030 Agenda for Sustainable Development adopted by the United Nations General Assembly in September 2015, Member States renewed their commitment to promote health and well-being of their populations.

A number of engagements at the UN led up to the SDGs. On 12 December 2012, the United Nations General Assembly endorsed a resolution⁷ on Global Health and Foreign Policy⁸ urging countries to accelerate progress toward universal health coverage (UHC) – the idea that everyone, everywhere should have access to quality, affordable health care - as an essential priority for international development then Member states also recognized that the importance of universal coverage in national health systems, especially through primary health-care and social protection mechanisms, to provide access to health services for all, in particular for the poorest segments of the population.

On 12 December 2017, the UN passed a third resolution on Global Health and Foreign Policy: addressing the health of the most vulnerable for an inclusive society⁹, which called on Member States to promote and strengthen their dialogue with other stakeholders, including civil society, academia and the private sector, in order to maximize their engagement in and contribution to the implementation of health goals and targets through an intersectoral and multi stakeholder approach.

Since 2017, 12 December has been proclaimed by the UN as International Universal Health Coverage Day (UHC Day)¹⁰. International Universal Health¹¹ Coverage Day aims to raise awareness of the need for strong and resilient health systems and universal health coverage with multi-stakeholder partners. Each year on 12 December, UHC advocates raise their voices to share the stories of the millions of people still waiting for health, champion what we have achieved so far, call on leaders to make bigger and smarter investments in health, and encourage diverse groups to make commitments to help move the world closer to UHC by 2030. The theme for the 2018 UHC Day was: "Unite for Universal Health Coverage: Now is the Time for Collective Action"¹².

United Nations General Assembly resolution 73/2 of 10 October 2018 on the political declaration of the third high-level meeting of the General Assembly on the prevention and control of non-communicable diseases, committed to promote increased access to affordable, safe, effective and quality medicines and diagnostics and other technologies, reaffirming the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement), as amended, and also reaffirming the Doha Declaration on the TRIPS Agreement and Public Health (2001), which recognizes that intellectual property rights should be interpreted and implemented in a manner WHA72.4 supportive of the right of Member States to protect public health and, in particular, to promote access to medicines for all, and which notes the need for appropriate incentives in the development of new health products,¹³.

⁷[\[http://undocs.org/A/RES/67/81\]](http://undocs.org/A/RES/67/81)

⁸[\[http://undocs.org/A/RES/67/81\]](http://undocs.org/A/RES/67/81)

⁹[\[http://undocs.org/A/RES/72/139\]](http://undocs.org/A/RES/72/139)

¹⁰[\[http://undocs.org/a/res/72/138\]](http://undocs.org/a/res/72/138)

¹¹[\[http://universalhealthcoverageday.org/\]](http://universalhealthcoverageday.org/)

¹²[\[http://universalhealthcoverageday.org/\]](http://universalhealthcoverageday.org/)

A high-level United Nations Political Declaration on universal health coverage (UHC) was adopted on September 23, 2019 and is the most comprehensive set of health commitments adopted till date. “This declaration represents a landmark for global health and development,” said Dr Tedros Adhanom Ghebreyesus, Director-General at WHO. “The world has 11 years left to make good on its sustainable development goals. Universal health coverage is key to ensuring that happens.” In adopting the declaration, U.N. Member States have committed to advance towards UHC by investing in four major areas around primary health care. These include mechanisms to ensure no one suffers financial hardship because they have had to pay for healthcare out of their own pockets and implementing high-impact health interventions to combat diseases and protect women’s and children’s health. In addition, countries must strengthen health workforce & infrastructure and reinforce governance capacity. They will report back on their progress to the U.N. General Assembly in 2023¹³.

The SDGs are the blueprint to achieve a better and more sustainable future for all. They address the global challenges by interconnecting in order to leave no one behind, it is important that we achieve each Goal and target by 2030¹⁴. Health and other SDGs are mutually reinforcing. The three core dimensions of UHC: population coverage, health services coverage and financial coverage are affected by health systems adversities. Health systems need to continuously adapt to provide appropriate and needed health services. To achieve and sustain UHC through health system strengthening, each country needs to forecast the likely impact of these megatrends on their health systems and adapt them accordingly. Addressing other SDGs can promote UHC, whereas achieving UHC can benefit other sector goals.

A number of the 17 SDGs of the 2030 Agenda apart from Goal 3 have health embedded in them. - The Sustainable Development Goal 3 is to “ensure healthy lives and promoting well-being for all at all ages”.

The goals within a goal: Health targets for SDG 3 are critical to public health care¹⁵. The target 3.8 that defines Universal Health Coverage (UHC) (Achieve universal health coverage, including financial risk protection, access to quality essential health care services and access to safe, effective, quality and affordable essential medicines and vaccines for all) is key to attaining Goal 3 in its entirety, as well as the health-related targets of other Sustainable Development Goals¹⁶. The targets are wide ranging and aim to reduce the global maternal mortality ratio; end preventable deaths of newborns and children; and also tackle communicable and non-communicable diseases¹⁷. The SDGs are founded on the principle that they are “integrated and indivisible” – progress in one area is dependent upon progress in many others. Translating this idea into practical action is one of the key challenges¹⁸.

“Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all”

Sustainable Development Goals 3.8

¹³<https://www.who.int/news-room/detail/23-09-2019-who-welcomes-landmark-un-declaration-on-universal-health-coverage>

¹⁴<https://www.un.org/sustainabledevelopment/sustainable-development-goals/>

¹⁵<https://www.who.int/topics/sustainable-development-goals/targets/en/>

¹⁶WHA72.14

¹⁷<https://www.un.org/sustainabledevelopment/health/>

¹⁸Achieve universal health coverage, including financial risk protection, access to quality essential health care services, and access to safe, effective, quality and affordable essential medicines and vaccines for all.

There is, of course, no “one size fits all” solution, and each country must walk its own path toward universal health coverage.

On September 24, 2019, at the United Nations General Assembly, 12 multilateral agencies launched the Global Action Plan, a joint plan to better support countries over the next 10 years to accelerate progress towards the health-related SDGs. Developed over 18 months, Stronger Collaboration, Better Health: Global Action Plan for Healthy Lives and Well-being for All outlines how a dozen multilateral health, development and humanitarian agencies will collaborate to be more efficient and provide more streamlined support to countries to deliver universal health coverage and achieve the health-related SDG targets¹⁹. Under the Global Action Plan, the agencies commit to strengthening their collaboration to:

- Engage with countries better to identify priorities, plan and implement together;
- Accelerate progress in countries through joint actions under 7 accelerator themes, which represent common challenges for many countries and where the agencies’ mandates, expertise and resources offer solutions, namely: 1) Primary health care 2) Sustainable health financing 3) Community and civil society engagement 4) Determinants of health 5) Innovative programming in fragile and vulnerable settings and for disease outbreak responses 6) Research and development, innovation and access, and 7) Data and digital health. They will also work together to advance gender equality and support the delivery of global public goods;
- Align by harmonizing their operational and financial strategies and policies in support of countries to increase efficiency and reduce the burden on countries; and
- Account, by reviewing progress and learning together to enhance shared accountability.

The work on a ‘Global Action Plan for Healthy Living and Well-being for All’ aims to ensure more effective and efficient use of resources and stronger, coherent support to countries for SDG3²⁰.

BOX 1: SDG 3 “Ensure healthy lives and promote wellbeing for all at all ages”

The goals within a goal: Health targets for SDG 3

3.1 By 2030, reduce the global maternal mortality ratio to less than 70 per 100 000 live births.

3.2 By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1000 live births and under-5 mortality to at least as low as 25 per 1000 live births.

3.3 By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases.

3.4 By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being.

3.5 Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol.

3.6 By 2020, halve the number of global deaths and injuries from road traffic accidents.

¹⁹<https://www.who.int/news-room/detail/24-09-2019-multilateral-agencies-launch-a-joint-plan-to-boost-global-health-goals>

²⁰<https://www.who.int/news-room/detail/24-09-2019-multilateral-agencies-launch-a-joint-plan-to-boost-global-health-goals>

3.7 By 2030, ensure universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes.

3.8 Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.

3.9 By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination.

3.a Strengthen the implementation of the WHO Framework Convention on Tobacco Control in all countries, as appropriate.

3.b Support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade-Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all.

3.c Substantially increase health financing and the recruitment, development, training and retention of the health workforce in developing countries, especially in least developed countries and small island developing States.

3.d Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks.

However, all concentrated efforts are necessary to make progress. The September 2019 United Nations (UN) Political Declaration recognized “that action to achieve universal health coverage by 2030 is inadequate and that the level of progress and investment to date is insufficient to meet target 3.8 of the Sustainable Development Goals, and that the world has yet to fulfil its promise of implementing, at all levels, measures to address the health needs of all” (Annex 1– UN Political declaration). Last year, 2018 marked the 40th anniversary of the Alma Ata Declaration, which set out a goal of achieving health for all for which, the world came together in Astana, Kazakhstan, at the Global Conference on Primary Health Care to renew a commitment to primary health care to achieve universal health coverage and the SDGs²¹.

Dr Antonio Guterres, the UN Secretary General (SG) has stated: “*Health is both an outcome and a driver of progress. It is at the centre of our vision of a more sustainable, inclusive, peaceful and prosperous future.*”

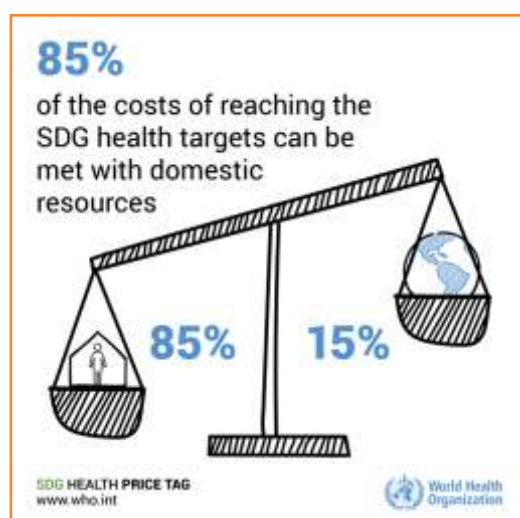
²¹<https://www.who.int/primary-health/conference-phc>

III. Universal Health Coverage: Moving Together to Build a Healthier World: Follow on to the United Nations General Assembly (UNGA) 2019

Universal Health Coverage in the Context of the Sustainable Development Goals

Universal Health Coverage (UHC) has a critical place in the SDG 2030 agenda. The goal of UHC is improved health. It includes the full spectrum of essential, quality health services, from health promotion to prevention, treatment, rehabilitation, and palliative care²². The key to accelerating progress towards better health is to provide accessible, quality essential health services without financial hardship to individuals, families and communities, thus enabling a transition to more productive and equitable societies and economies.

Universal health coverage is both a goal in itself and a means for implementing other goals. It is crucial for tackling public health problems, in particular to ensure health system responses. The achievement of universal health coverage also holds potential for disease prevention and health promotion²³. Scaling up the implementation of public health interventions is therefore clearly the key to achieving universal health coverage.



Progress towards universal health coverage is a continuous process. Target 3.8 has two indicators:

- 3.8.1 on coverage of essential health services and
- 3.8.2 on the proportion of population with large household expenditures on health.

These indicators represent the latest efforts to monitor the world's path towards universal health coverage²⁴.

Universal health coverage efforts in this area focus on two issues: “catastrophic spending on health”, which is out-of-pocket spending (without reimbursement by a third party) that exceeds a household's ability to pay; and “impoverishing spending on health”, which occurs when a household is forced by an adverse health event to divert spending away from non-medical budget items, such as food, shelter and clothing, to such an extent that it is considered to be living below the poverty line. The incidence of catastrophic spending on health is reported in terms of two thresholds: out-of-pocket expenditures that exceed 10% of household total income or consumption and those that exceed 25%. This is the approach adopted for the SDGs monitoring framework.

²²[https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-\(uhc\)](https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc))

²³See Box [https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-\(uhc\)](https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc))

²⁴WHA72/14

BOX 2: What UHC is not

There are many things that are not included in the scope of UHC:

- UHC does not mean free coverage for all possible health interventions, regardless of the cost, as no country can provide all services free of charge on a sustainable basis.
- UHC is not just about health financing. It encompasses all components of the health system: health service delivery systems, the health workforce, health facilities and communications networks, health technologies, information systems, quality assurance mechanisms, and governance and legislation.
- UHC is not only about ensuring a minimum package of health services, but also about ensuring a progressive expansion of coverage of health services and financial protection as more resources become available.
- UHC is not only about individual treatment services, but also includes population-based services such as public health campaigns, adding fluoride to water, controlling mosquito breeding grounds, and so on.
- UHC is comprised of much more than just health; taking steps towards UHC means steps towards equity, development priorities, and social inclusion and cohesion.

During the UN General Assembly (UNGA) meeting on Universal Health Coverage, WHO and partners-World Bank, the Organisation for Economic Co-operation and Development, the United Nations Population Fund, and UNICEF, launched the Biennial report on Universal Health Coverage Global Monitoring Report 2019 titled 'Global Monitoring Report on Financial Protection in Health 2019'²⁵. The Report states that countries must increase spending on primary healthcare by at least 1% of their gross domestic product (GDP) if the world is to close glaring coverage gaps and meet health targets agreed in 2015²⁶. Members must also intensify efforts to expand services countrywide. The world will need to double health coverage between now and 2030, according to the Universal Health Coverage Monitoring Report. The report warns that if current trends continue, up to 5 billion people will still be unable to access health care in 2030 – the deadline world leaders have set for achieving universal health coverage. Most of those people are poor and already disadvantaged.

It has been stated to address the multi-sectoral nature of health determinants, the health sector should promote “Health in All Policies”- an approach to public policies across sectors that systematically takes into account the health implications of decisions, seeks synergies and avoids harmful health impacts in order to improve population health and health equity, and address the social determinants of health. Areas of particular relevance include trade and intellectual property, sustainable energy, income inequality, migration, food security, and sustainable consumption and production. This will require revisiting and reshaping the architecture for global health, particularly in relation to health security and the development of global public goods.

²⁵Global Monitoring Report on Financial Protection in Health 2019, https://www.who.int/healthinfo/universal_health_coverage/report/fp_gmr_2019.pdf?ua=1

²⁶https://www.who.int/healthinfo/universal_health_coverage/report/uhc_report_2019.pdf?ua=1

Primary Health-Care focus for UHC

UHC requires a strong primary health-care focus, promoting the individual's engagement in their health, and assuring community-level access to the full spectrum of services, from health promotion and prevention to treatment, rehabilitative and palliative care²⁷.

Primary health care is an approach to health and wellbeing centred on the needs and circumstances of individuals, families and communities. It addresses comprehensive and interrelated physical, mental and social health and wellbeing.

It is about providing whole-person care for health needs throughout life, not just treating a set of specific diseases. Primary health care ensures people receive comprehensive care, ranging from promotion and prevention to treatment, rehabilitation and palliative care as close as feasible to people's every day environment.

WHO has developed a cohesive definition of primary health care based on three components:

- ensuring people's health problems are addressed through comprehensive promotive, protective, preventive, curative, rehabilitative, and palliative care throughout the life course, strategically prioritizing key system functions aimed at individuals and families and the population as the central elements of integrated service delivery across all levels of care;
- systematically addressing the broader determinants of health (including social, economic, environmental, as well as people's characteristics and behaviours) through evidence-informed public policies and actions across all sectors; and
- empowering individuals, families, and communities to optimize their health, as advocates for policies that promote and protect health and wellbeing, as co-developers of health and social services through their participation, and as self-carers and care-givers to others.

Primary health care is the most efficient and cost effective way to achieve universal health coverage around the world²⁸.

The importance of primary health care (PHC) has also been acknowledged in the declaration issued by the 2018 Meeting of G20 Health Ministers. PHC has also been recognized in the 2019 UNGA political declaration on UHC: "primary health care brings people into first contact with the health system and is the most inclusive, effective and efficient approach to enhance people's physical and mental health, as well as social well-being, and that primary health care is the cornerstone of a sustainable health system for universal health coverage and health-related Sustainable Development Goals, as was declared in the Declaration of Alma-Ata and reaffirmed by the Declaration of Astana".

Primary health care services rely on access to health products, including medicines, vaccines, medical devices, diagnostics, protective equipment and assistive devices. These products must be of assured safety, efficacy, performance and quality, as well as being appropriate, available and affordable. Ensuring that appropriate health products are available and affordable for primary care depends on policy decisions and processes related to the selection, pricing, procurement, supply chain management, maintenance (in the case of medical devices), prescribing and dispensing (in the case of medicines) and use of health products.

²⁷Reich MR, Harris J, Ikegami N, Maeda A, Cashin C, Araujo EC, et al. Moving towards universal health coverage: lessons from 11 country studies. *The Lancet*. 2016; 387:811-16 ([https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(15\)60002-2.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(15)60002-2.pdf)).

²⁸[https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-\(uhc\)](https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc))

Ministers of health gathered at the World Health Assembly (WHA) agreed on four resolutions related to the SDGs and UHC, addressing

- Implementation of the 2030 Agenda for Sustainable Development- WHA72.11 Rev.1²⁹
- Universal health coverage: Primary health care towards universal health coverage- WHA72.12³⁰
- Universal health coverage: Community health workers delivering primary health care: opportunities and challenges, WHA72.13³¹
- Universal health coverage: Preparation for the high-level meeting of the United Nations General Assembly on universal health coverage, WHA72.14

In addition certain other resolutions such as Follow-up to the high-level meetings of the United Nations General Assembly on health-related issues Prevention and control of noncommunicable diseases (NCDs), (WHA72.19)³² also stressed the role of health systems to address NCDs through people-centred primary health care and universal health coverage, building on guidance set out in WHO's Global action plan for prevention and control of noncommunicable diseases.

Thirteenth General Programme of Work

As part of WHO's contribution both to the achievement of the 2030 Agenda for Sustainable Development, and to the promotion of a coordinated multisectoral approach to implement the Sustainable Development Goals, the WHO developed the Thirteenth General Programme of Work, 2019–2023. WHO worked with other international organizations to develop a “global action plan for healthy lives and well-being for all” with the aim of providing better support to Member States in their efforts to achieve the health - related Sustainable Development Goals, including target 3.8 on universal health coverage³³.

“Universal health coverage is ultimately a political choice. It is the responsibility of every country and national government to pursue it. It is more of a political than an economic challenge”

- Dr Tedros Adhanom Ghebreyesus, WHO Director-General

The Thirteenth General Programme of Work, 2019–2023 sets out three strategic priorities for ensuring healthy lives and well-being for all at all ages:

- achieving universal health coverage,
- addressing health emergencies and
- promoting healthier populations.

These strategic priorities are supported by three strategic shifts: stepping up leadership; driving health impact in every country; and focusing global public goods on impact³⁴.

²⁹https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_11Rev1-en.pdf

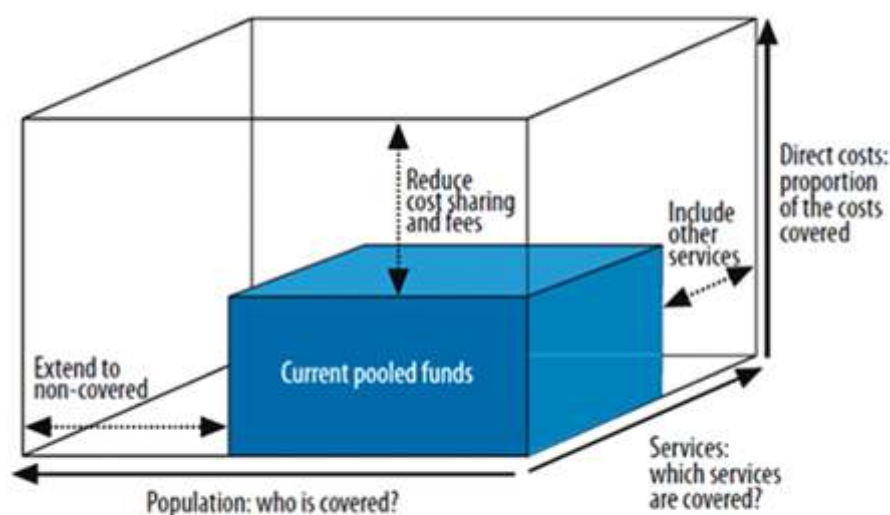
³⁰https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_12-en.pdf

³¹https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_13-en.pdf

³²https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_19-en.pdf

³³Document A71/12. Annex A72/17

³⁴Thirteenth General Programme of Work 2019–2023 (<http://www.who.int/about/what-we-do/gpw-thirteen-consultation/en/>)



Three dimensions to consider when moving towards universal coverage

Promoting Equitable Access for SDGs

Equitable access to health products is a global priority, and the availability, accessibility, acceptability, and affordability of health products of assured quality need to be addressed in order to achieve the SDGs, in particular target 3.8.1. Every disease management strategy requires access to health products for prevention, diagnosis, treatment, palliative care and rehabilitation.

Access is a global concern, given the high prices of new pharmaceuticals and rapidly changing markets for health products that place increasing pressure on all health systems' ability to provide full and affordable access to quality health care. The high percentage of health spending on medicines (20–60% as demonstrated in a series of studies in selected low- and middle-income countries) impedes progress for the many countries that have committed to the attainment of universal health coverage. Furthermore, it is known that a large proportion of the population in low-income countries who spend for health do pay out-of-pocket for medicines. With the rise in non-communicable diseases – many of which are chronic conditions that require long-term treatment – the financial burden on both governments and patients will become even greater³⁵

Improving access to health products is a multidimensional challenge that requires comprehensive national policies and strategies. These should align public health needs with economic and social development objectives and promote collaboration with other sectors, partners and stakeholders; they also need to be aligned with legal and regulatory frameworks and cover the entire product life cycle, from research and development to quality assurance, supply chain management and use⁹.

Equitable access to health products is a global priority, and the availability, accessibility, acceptability, and affordability of health products of assured quality need to be addressed in order to achieve the Sustainable Development Goals, in particular target 3.8.1. Every disease management strategy requires access to health products for prevention, diagnosis, treatment, palliative care and rehabilitation.

³⁵WHA72.17 (2019) Draft Road Map for Access To Medicines, Vaccines And Other Health Products, 2019–2023 (http://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_17-en.pdf)

Roadmap for access 2019-2023- Comprehensive support for access to medicines and vaccines

Assuring access to medical products is key to advancing UHC. The World Health Assembly adopted decision WHA71(8), which led to road map³⁶ 2019–2023 for access to medicines, vaccines and other health products.

The draft road map has been revised and a new Appendix 2 has been added to indicate the linkage between the Thirteenth General Programme of Work, 2019-2023 and the activities, actions, deliverables and milestones set out in the road map.

The roadmap developed for Access to medicines and vaccines has the following parameters:

1. Research and development for medicines and vaccines that meets public health needs
2. Fair pricing and financing policies
3. Application and management of intellectual property to contribute to innovation and promote public health
4. Procurement and supply chain management
5. Appropriate prescribing, dispensing and use
6. Regulatory systems that ensure quality, safety and efficacy of medicines and vaccines
7. Preparedness for emergencies
8. Good governance
9. Collecting, monitoring and using key data
10. Health workforce capacity for access to medicines and vaccines areas to be addressed during 2019-2023

WHO South-East Asia Region (SEAR): Access to essential medical products

In the WHO South-East Asia Region (SEAR), access to essential medicines is a priority in the Regional Flagship on UHC. Access to medicines has been continuously engaging the Member States in the Region. As an intervention, to improve access to quality essential medicines, South East Asia Region also renewed and firmed up its commitment in 2018 by signing Delhi Declaration by Honorable Health Ministers. The Health Ministers of the Member States of the WHO SEAR, participating in the 71st session of the WHO Regional Committee for SEAR at New Delhi, India adopted the Delhi Declaration on 'Improving access to essential medical products in the South-East Asia Region and beyond'³⁷.



³⁶WHA72.17 (2019) Draft Road Map For Access To Medicines, Vaccines And Other Health Products, 2019–2023 (http://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_17-en.pdf)

³⁷Delhi Declaration on 'Improving access to essential medical products in the South-East Asia Region and beyond' (<https://apps.who.int/iris/bitstream/handle/10665/274331/Delhi-Declaration.pdf?sequence=5&isAllowed=y>)

The National Health Policy, 2017³⁸ has specified targets for universalising primary health care, achieving further reductions in infant and under-5 mortality, preventing premature deaths due to non-communicable diseases as well as increasing government expenditure on health. A composite index is being used to monitor and incentivise improvements in health services delivery across states in the country. The government is aiming to immunize all unimmunized and partially immunized children against vaccine preventable diseases by 2020.

NITI Aayog, the policy think-tank of the Government of India, in keeping with its mandate to foster stakeholder involvement and coordinate the achievement of the Sustainable Development Goals, has initiated a series of consultations called the 'Development Dialogues'. As a part of its health agenda, NITI Aayog has, over last one year, facilitated several dialogues and conversations amongst Indian and global academia and researchers to provide an in-depth analysis and diagnosis and reflections on the key building blocks of the Indian health system.

India, over the years, has made significant improvements in increasing life expectancy, reducing child and maternal mortality and tackling other existing and emerging health priorities. Further, there is a strong political commitment towards achieving the SDGs of Good Health and Well-being for all Indians by 2030, which is articulated and strategized in the National Health Policy of 2017. In line with the SDG framework for achieving universal health coverage, financial risk protection, and access to essential quality health care services, the Government of India has initiated several reforms within its health system.

The Government of India is committed to a robust regulatory system for ensuring safety, quality and efficacy of medical products. Regulators play a critical role – also in informing manufacturers for best practices. Effective regulatory systems are an essential component of health system strengthening for better public health outcomes. The Central Drugs Standards Control Organization (CDSCO) the Central level and provincial State Regulatory Agencies come together every year in an Annual Regulators Conclave to promote equitable access to quality, safe, efficacious, and affordable medical products.

The AYUSHMAN Bharat program envisions providing comprehensive health care to reduce out-of-pocket expenditure and to promote overall health and well-being of the population. This bold reform aims to strengthen access to integrated and high-quality secondary and tertiary health care while also focusing on preventive and primary health services.

Towards achieving universal health coverage, a health insurance cover of INR 100,000 (USD 1,563) is being extended to all poor families. Ayushman Bharat³⁹ is arguably the largest public health initiative in the world planning to cover 100 million families across the country. The



³⁸<https://mohfw.gov.in/sites/default/files/9147562941489753121.pdf>

³⁹<https://www.abnhpm.gov.in/>

scheme has two main components: one that envisages the transformation of 1,50,000 primary healthcare centres and sub-centres into “wellness centres” that would lay stress on prevention of illness, and second, a health insurance package of INR 5 lakh (approximately USD 7000 USD) for each of the 100 million families being covered. Other major programs like Transformation of Aspirational Districts, National Nutrition Mission (POSHAN Abhiyan), and the Swachh Bharat Mission are playing an important role in meeting the Sustainable Development Goals. To implement these reforms well, there is a need for continuous engagement between the government and different stakeholders from across the health care ecosystem to realize a long-term vision towards building strong supporting institutional systems.

“Universal Health for all, a disease free India and global standards of excellence in healthcare is our aim for a new India”, said Dr Harsh Vardhan, Union Minister, Ministry of Health and Family Welfare at 72nd Session of Regional Committee Meeting for SEAR. The Health Minister reiterated the Prime Minister’s commitment, to the health of India’s citizens to deliver affordable and inclusive healthcare for all.

Through Ayushman Bharat India is establishing 1,50,000 Health and Wellness centres by the year 2022, which shall provide an entire gamut of preventive healthcare. The second component, Pradhan Mantri Jan Arogya Yojana, is aimed at providing health protection cover to over 100 million poor and vulnerable families for secondary and tertiary care including pre- and post- hospitalisation expenses. Key features include health cover of upto Rs 5 hundred thousand per family. A total of 17000 hospitals have been empanelled so far under this scheme. More than 4.1 million persons have become beneficiaries under this scheme and have saved a total of approximately 120 billion INR on health expenditure.

Availability of Medical products (medicines, vaccines, devices, diagnostics): India’s National Health Policy accords special focus on production of Active Pharmaceutical Ingredients (API) which is necessary for the generic formulations industry. The policy recognizes the need to regulate the use of medical devices so as to ensure safety and quality compliance as per the standard norms. Recognizing that over 70% of the medical devices and equipments are imported in India, the policy advocates the need to incentivize local manufacturing to provide customized and affordable indigenous products for Indian population in the long run. The goal with respect to medical devices is to encourage domestic production in consonance with the “Make in India” national agenda. Medical technology and medical devices have a multiplier effect in the costing of healthcare delivery.

VI. Funding and Investments in Medical Products R&D: Role of Data Tracking Initiatives

Each year, hundreds of billions of dollars are spent on research and development (R&D) into new or improved health products and processes, ranging from medicines to vaccines to diagnostics. Effective knowledge sharing, collaboration and coordination between funding organizations, regulators, public as well as private sector is needed to improve responses to epidemics and ensure that identified R&D gaps are filled effectively. It is also agreed that epidemiological and clinical research should be incorporated under the umbrella of the coordination mechanism, with product R&D before and during public health emergencies⁴⁰. Ensuring that decision-making about which diseases, countries and products receive investment funds is not entirely reliant on market forces is critical.

The public sector invests in providing essential medicines for effective healthcare delivery, but it also supports the basic, clinical and translational research, and the training of the scientific staff that lead to the development of such products. However, various issues have flagged the importance of ensuring fair returns on public investments in R&D. Repeated assessments have noted the considerable contribution of government funding towards the research behind health technology products. It can take ten to fifteen years for drugs to emerge from the R&D pipeline. Innovation can be unnecessarily slowed when pre-clinical findings are kept secret even after these drug products have been shelved. Failing to share both pre-clinical as well as clinical trial findings results in wasting research funding and chasing unfruitful leads.

At multiple points in the pharmaceutical value chain, non-transparency can have negative consequences, both for patients and for the pace of drug innovation. When the answers are known from previously undisclosed clinical trials, patients are put at unnecessary risk if they have to volunteer to repeat such testing. Hidden R&D costs and unclear intellectual property holdings make it challenging to quantify fair returns on R&D to industry partners⁴¹.

The 2014 outbreak of Ebola virus disease in West Africa, provided important lessons and exposed the lack of investments in products and approaches to prevent and minimize the impact of pathogens with epidemic potential. Gaps in R&D investments in the pipeline for antimicrobial medicines are a cause of global concern in the context of rapidly increasing antimicrobial resistance.

WHO Global Observatory on Health R&D

In 2017, the World Health Organization (WHO) launched a new initiative - 'Global Observatory on Health R&D' to gather information and provide an accurate picture of where and how R&D investments are being made, helping governments, funders and researchers to make better decisions on investment and policy making priorities⁴². The initiative is the result of resolution WHA66.22 to help identify health R&D priorities based on public health needs⁴³, by:

⁴⁰<https://www.chathamhouse.org/sites/default/files/events/2016-11-10-Global-Coordination-Meeting-Summary.pdf>

⁴¹Anthony So, Professor of the Practice at Johns Hopkins Bloomberg School of Public Health and Head of the ReAct–Strategic Policy Program (aso5@jhu.edu)

⁴²<https://www.who.int/features/2018/health-research-and-development/en/>

⁴³https://www.who.int/research-observatory/why_what_how/en/

- consolidating, monitoring and analyzing relevant information on the health R&D needs of developing countries;
- building on existing data collection mechanisms; and
- supporting coordinated actions on health R&D.

The WHO Global Observatory on Health R&D has identified striking gaps and inequalities in investment both between countries and between health issues, with frequent disconnects between burden of disease and level of research activity. High income countries have an average of 40 times more health researchers than low income countries. Investing in R&D to discover and develop medicines and vaccines is key to improving access to medicines and quality health care for people across the world and to achieving universal health coverage. The Global Health Observatory on Health R&D builds on existing data and reports from a wide range of sources as well as newly gathered information to provide an accurate picture of the current investment situation and enable informed decision making on priorities⁴⁴.

G-Finder Survey

G-Finder Survey, funded by the Bill & Melinda Gates Foundation, and conducted by Policy Cures Research, tracks public, private, and philanthropic funding of basic research and product development (R&D) for global health priorities, particularly neglected diseases in LMICs⁴⁵. G-Finder reports include data on all types of product-related R&D, including basic research, discovery and pre-clinical, clinical development, Phase IV and pharmacovigilance studies, and baseline epidemiological studies. Product gaps, needs, market failure are the criteria for neglected diseases in G-Finder; and its data is used as the primary source of neglected disease R&D funding data for WHO Global Observatory on Health R&D⁴⁶. The drug development portfolio of the Drugs for Neglected Diseases initiative (DNDi) is also aligned with the findings of G-Finder⁴⁷. G-Finder also tracks funding for emerging infectious diseases (EIDs), and sexual and reproductive health (SRH) issues.

World RePORT

World RePORT is an interactive, open-access online database and mapping tool of global research investments hosted by National Institutes of Health, USA. The tool depicts direct and indirect awards supported by some of the world's largest biomedical research funders by continent, country, funding organization, research organization and year. It includes funding data from 2012 through 2017. World RePORT provides a public means to track international research activities and partnered investments, increase awareness of funding opportunities and share results with the broader research and funding community. The goal is to improve understanding of the research landscape, identify gaps in funding and areas where there might be a duplication of effort, and enable funders to more effectively synergize investments⁴⁸.

International Initiatives

Several international and national public and non-profit organizations are investing in specific areas of healthcare. UNITAID invests in innovations to prevent, diagnose and treat HIV/AIDS, tuberculosis and malaria more quickly, affordably and effectively⁴⁹. An entrepreneurial organization, PharmAccess Foundation has a digital agenda dedicated to connecting more

⁴⁴<https://www.who.int/features/2018/health-research-and-development/en/>

⁴⁵<https://gfinder.policycuresresearch.org/>

⁴⁶https://www.who.int/research-observatory/monitoring/inputs/neglected_diseases/en/

⁴⁷https://www.dndi.org/wp-content/uploads/2018/08/DNDi_AR_2017.pdf

⁴⁸<https://www.fic.nih.gov/Global/Pages/world-report-interactive-global-biomedical-research-mapping.aspx>

⁴⁹<https://unitaid.org/about-us/#en>

people to better healthcare in Africa⁵⁰. Investments in Product Development Partnerships (PDPs) are also being made through initiatives for access to medicines⁵¹. There are collaborative initiatives such as ‘The Access to Medicine Index’ supported by the BMGF and the UK and Dutch governments, that independently ranks pharmaceutical companies’ efforts to improve access to medicine in developing countries⁵². Grand Challenges initiatives of the BMGF also foster innovation to solve key global health and development problems⁵³.

India Initiatives

In India, Grand Challenges initiatives are being steered by the Department of Biotechnology (DBT) through an umbrella Memorandum of Understanding (MOU) with BMGF for mission-directed research and build Grand Challenges India to support health research and innovation. The MOU aims to support initiatives that could dramatically change the health and development landscape in India and other countries facing similar challenges⁵⁴. India has also entered into collaboration with UK for strengthening healthcare delivery through AI and digital health⁵⁵.

The various initiatives for tracking investments in health R&D provide a better understanding of current investment trends; products in the pipeline and clinical trials; country and disease specific information such as burden of disease; global indicators on health R&D in the context of the SDGs. The publications, databases, classifications, standards and other resources of these tracking initiatives facilitate discussions and consensus to harmonize approaches to collect and share R&D data. The available information is required to be leveraged to its optimum potential, leading to bridging of the gaps and facilitating policy initiatives, thereby providing improved access to medical products.



⁵⁰<https://www.pharmaccess.org/>

⁵¹<https://www.mmv.org/partnering/other-product-development-partnerships-pdps>

⁵²<https://accesstomedicineindex.org/>

⁵³<https://gcgh.grandchallenges.org/>

⁵⁴http://www.birac.nic.in/desc_new.php?id=103

⁵⁵https://mea.gov.in/bilateraldocuments.htm?dtl/29831/IndiaUK_List_of_MOUsAgreementsInitiatives_during_the_visit_of_Prime_Minister_to_UK_London_April_18_2018

V. Incentives for Development in Antibiotics, Global AMR R&D Hub

The vision of UHC is that all people should have access to the services they need without facing financial hardship. Ensuring equitable access to appropriate and affordable antimicrobial medicines is a fundamental part of that vision.

Antimicrobial resistance is putting the gains of the Millennium Development Goals at risk and endangers achievement of the Sustainable Development Goals. Antimicrobial resistance happens when microorganisms (such as bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics). Microorganisms that develop antimicrobial resistance are sometimes referred to as “superbugs”. As a result, the medicines become ineffective and infections persist in the body, increasing the risk of spread to others.

Without effective antimicrobials for prevention and treatment of infections, medical procedures such as organ transplantation, cancer chemotherapy, diabetes management and major surgery (for example, caesarean sections or hip replacements) become very high risk. Antimicrobial resistance increases the cost of health care with lengthier stays in hospitals and more intensive care required⁵⁶.

Antibiotics, antivirals, antiparasitic agents and antifungals are increasingly ineffective owing to resistance developed through their excessive or inappropriate use, with serious consequences for human and animal health, and possibly for plant health, and negative impacts on food, the environment and the global economy.

While AMR has the highest burden in low to middle income countries, high income countries are also greatly affected. In fact, around 2.4 million people could die in high income countries between 2015 and 2050 without a sustained effort to contain AMR. Addressing AMR will be key to achieving Universal Health Coverage and meeting the Sustainable Development Goals⁵⁷.

Antibiotics have been a critical tool since the discovery of penicillin in 1928, saving the lives of millions of people and animals around the world. The increasing emergence and spread of antimicrobial resistance (AMR) over the last few decades is reducing the efficacy of these lifesaving drugs and is now a major threat to global health. This, coupled with the lack of new treatments, preventive measures, diagnostics and alternatives to antimicrobials emerging from the clinical pipeline, has emphasized that urgent and coordinated action is required. This critical issue has been discussed in many countries



and at international fora including the United Nations General Assembly (UNGA), the World Health Assembly (WHA), the G7 and the G20 resulting in high political interest and commitment.

⁵⁶<https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>

⁵⁷<https://www.gardp.org/rd-strategy/5by25/>

WHO global strategy for containment of AMR

In 2001, WHO adopted a global strategy for containment of AMR, which followed resolutions from the World Health Assembly dating back to 1984. In May 2015, the World Health Assembly endorsed a global action plan on AMR (WHA68.7) to tackle antimicrobial resistance. The plan follows the One Health approach, looking at actions on human and animal health care areas, the food chain and the environment⁵⁸.

Further, WHO's Global Action Plan on Antimicrobial Resistance (GAP-AMR) combines new medicines, discovery development and stewardship (WHO Secretariat (2016) Global action plan on antimicrobial resistance (A69/24 Add.1). This initiative draws its strength from both: WHO's mandate to drive the global response to antimicrobial resistance and set health priorities, and DNDi's expertise in harnessing partnerships to develop new antibiotics and build a pipeline for neglected diseases and deliver not-for-profit, needs-driven R&D for resource-limited settings.

The recent 2019 72nd WHA adopted a Resolution on antimicrobial resistance⁵⁹. There is a commitment to mobilize adequate, predictable and sustained funding and human and financial resources and investment through national, bilateral and multilateral channels to support the development and implementation of NAPs, research and development on existing and new antimicrobial medicines, diagnostics and vaccines, and other technologies, and strengthening of related infra-structure⁶⁰.

The progress in implementing the Global Action Plan has five main objectives:

Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

Objective 2: Strengthen the knowledge and evidence base through surveillance and research

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

Objective 4: Optimize the use of antimicrobial medicines in human and animal health

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

The Objectives 2, 4 and 5 are focused on research for AMR.

The 'Political Declaration of the High-Level Meeting of the UNGA on Antimicrobial Resistance' adopted at the United Nations General Assembly resolution 71/3 (2016) provides the basis for a sustained commitment of all United Nations (UN) Members at the highest political level, by linking action against AMR to the achievement of the 2030 Agenda for Sustainable Development⁶¹.



⁵⁸ Global action plan on antimicrobial resistance - https://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_R7-en.pdf

⁵⁹ Follow-up to the high-level meetings of the United Nations General Assembly on health-related issues Antimicrobial resistance-WHA72.18

⁶⁰ WHA72/18

⁶¹ <https://sdg.iisd.org/news/unga-adopts-political-declaration-on-antimicrobial-resistance-discusses-links-with-sdgs/>

Support to AMR by the G20

The G20 is continuing its work in support of coordinated responses to global health issues to advance progress towards the SDGs, demonstrating a strong political commitment to tackle such challenges through global actions. In 2016, Antimicrobial resistance (AMR) was included for the first time in the G20 Leader's Communiqué of the Hangzhou Summit. In 2017, the G20 expressed its support to move towards universal health coverage (UHC) and discussed ways to strengthen the prudent use of antimicrobials and to boost the pharmaceutical R&D pipeline. They called for a new international R&D Collaboration Hub to maximize the impact of existing and new research initiatives as well as product development⁶². At the G20 health ministers' summit during the 2017 German G20 presidency, the Berlin Declaration was adopted which calls for urgent action and lays out a framework for possible next steps including strong interagency collaboration, thorough monitoring and stewardship to prevent over- and misuse of antibiotics, and fostering national and integrated regional action plans based on a One Health approach that sets out to acknowledge the interrelation of the health of humans, animals and ecosystems by covering multiple relevant working areas, and food safety in particular⁶³.

The Declaration welcomed new initiatives, including Global Antibiotic Research and Development Partnership (GARDP), a non-profit partnership of the WHO and the Drugs for Neglected Disease Initiative (DNDi) which can "reinvigorate research and development in science and industry for antimicrobials." It recognized the importance of reactivating the R&D pipeline through incentive mechanisms that do not rely on high price/volume combinations and that promote appropriate use of antibiotics.

The UN Secretary General has called on interested G20 members and Global AMR R&D Hub to analyze push and pull mechanisms to identify best models for AMR R&D and to report back to relevant G20 Ministers.⁶⁴ Furthermore, as new and remaining antibiotic developers struggle to mobilize financial resources, a coordinated effort between actors spanning research and development through to sustainable access is urgently needed to ensure both new and improved antibiotics remain available and effective to those who need them for generations to come⁶⁵. For several decades now, the pharmaceutical R&D pipeline has suffered from a paucity of novel classes of antibiotics. In the 1950s, there were nine newly discovered antibiotic classes⁶⁶. Each decade since then saw a decline in the discovery of novel classes. From 1990 to 2010, there were zero new classes of antibiotics discovered. These figures highlight the current scientific barriers to discovering innovative antibacterial agents. However, in 2017, the World Health Organization identified that five of the thirty-three new chemical entities for pathogens on their Priority Pathogens List had come from chemical classes not previously used in human medicine. Nonetheless, the situation is still far from promising. The average development time is seven years, and there is an approximately 15% chance of an antibiotic in a Phase 1 trial gaining market approval⁶⁷. These new antibiotics may come too late considering that already drug-resistant infections claim 700,000 lives each year globally⁶⁸.

⁶²https://www.g20.org/pdf/documents/en/annex_11.pdf

⁶³<http://www.g20.utoronto.ca/2017/170520-health-en.html>

⁶⁴https://www.g20.org/pdf/documents/en/FINAL_G20_Osaka_Leaders_Declaration.pdf

⁶⁵<https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>

⁶⁶Silver LL. Challenges of Antibacterial Discovery. Clin Microbiol Rev. 2011 Jan 1;24(1):71–109.

⁶⁷Antibacterial agents in clinical development: an analysis of the antibacterial clinical development pipeline, including tuberculosis [Internet]. Geneva: World Health Organization; 2017 [cited 2019 Jul 22]. Available from: <https://apps.who.int/iris/bitstream/handle/10665/258965/WHO-EMP-IAU-2017.11-eng.pdf?sequence=1>

⁶⁸Anthony So, Professor of the Practice at Johns Hopkins Bloomberg School of Public Health and Head of the ReAct–Strategic Policy Program

It has been seen that the private sector, however, is largely unwilling to take on the financial risk of developing new antibiotics that could help, as they bring little profit. The recent example is Achaogen, a San Francisco biotech that won one of the first antibiotic approvals in decades last year. Despite its novelty, plazomicin (Zemdri) generated sales less than \$1 million; Achaogen filed for bankruptcy just a few weeks ago⁶⁹.

Antimicrobial resistance: HIV, tuberculosis, malaria, neglected tropical diseases and sexually transmitted infections

According to the Global tuberculosis report 2018, drug-resistant tuberculosis continues to be a public health crisis. The best estimate is that, worldwide in 2017, 558,000 people developed tuberculosis that was resistant to rifampicin, the most effective first-line drug, of whom 82% had multidrug-resistant tuberculosis. Among cases of multidrug-resistant tuberculosis in 2017, 8.5% were estimated to have extensively drug-resistant tuberculosis. In July 2018, the latest evidence of the treatment of drug-resistant tuberculosis was reviewed by an independent panel of experts convened by WHO. A rapid communication on key changes to recommendations for the treatment of multidrug- and rifampicin-resistant tuberculosis was issued by WHO in August 2018 and outlined the reprioritization of medicines used in treatment, including the use of bedaquiline and replacing toxic injectables, with all-oral regimens as the standard of care⁷⁰.

The Global Technical Strategy for malaria 2016-2030 calls on countries and global malaria partners to monitor the efficacy of antimalarial medicines so that the most appropriate treatments can be selected for national policies. WHO continues to update the global database on antimalarial drug efficacy and resistance, which serves as the source for the therapeutic efficacy studies summary tables, the Malaria Threats Map and the WHO World malaria report.

The elimination of HIV/ AIDS as a public health threat calls for expansion of the coverage and quality of treatment and antiretroviral therapy services. This expansion needs to be balanced by efforts to ensure that the risks and impact of HIV drug resistance are minimized. WHO's HIV drug resistance report 2017 highlights trends of concern in the levels of HIV drug resistance across several regions. WHO has also linked the results of the reports on increasing pretreatment HIV drug resistance to new treatment guidelines which support the use of dolutegravir rather than efavirenz as part of the three-drug first-line treatment for HIV.

The Working Group on Monitoring of Neglected Tropical Diseases Drug Efficacy was established by WHO in 2011 due to the high treatment coverage rates for neglected tropical diseases in sub-Saharan Africa and South-East Asia. These high rates are expected eventually to contribute to the emergence of resistance to anthelmintic medicines; the Working Group's seventh meeting in 2018 articulated such concerns in relation to resistance to treatment for soil-transmitted helminthiasis. While anthelmintic resistance is problematic within the veterinary sector, the full scope of the problem in human helminthiasis is being studied; however, alternative anthelmintic medicines, for use alone or in combination, are needed in order to prevent resistance developing.

Resistance of sexually transmitted infections, in particular gonorrhoea (estimated at 78 million new infections per year), to antibiotics has increased rapidly in recent years and reduced treatment options. The emergence of decreased susceptibility of gonorrhoea to the last-line treatment option – namely, oral and injectable cephalosporins – combined with antimicrobial resistance already shown to penicillins, sulfonamides, tetracyclines, quinolones and

⁶⁹<https://endpts.com/once-picked-as-a-500m-winner-bankrupt-achaogen-auctions-off-its-antibiotic-for-a-fraction-of-that/>

⁷⁰https://www.who.int/tb/publications/global_report/en/

macrolides, make gonorrhoea a multidrug-resistant organism. WHO has issued new treatment guidelines for syphilis, gonorrhoea and chlamydia in order to address the problem of resistance to antibiotics.

“AWaRe” framework

To optimize the use of antimicrobial medicines in human and animal health- in its Model List of Essential Medicines (2019), WHO adopted a new classification for antibiotics to guide optimal use of antibiotics and reduce resistance, comprising three groups: (a) Access antibiotics; (b) Watch antibiotics; and (c) Reserve antibiotics. WHO anticipates that the introduction of the “AWaRe” framework will reduce the use of antibiotics in the Watch and Reserve groups, while the accessibility of those in the Access group will expand. Furthermore, all newly registered antibiotics will be reviewed and classified in AWaRe categories to guide stewardship programmes and define research gaps in the definition of their role in therapy.

One Health Strategy

To address AMR, a comprehensive and multifaceted strategy implemented across the One Health continuum is required. A fundamental component of any strategy to address AMR is increasing basic research and translational studies to support the development of new treatments, preventive measures, diagnostics and alternatives to antimicrobials. The importance of fostering research and development (R&D) to address AMR by international R&D Collaborations to maximize the impact of existing and new basic and clinical antimicrobial research initiatives as well as product development.

Economic impact of AMR

In a recent study to quantify the projected impact of drug resistance on the global economy between 2017 and 2050, the World Bank conducted economic simulations on the basis of low- and high-impact scenarios of antimicrobial resistance. In the scenarios, low-income countries experienced larger declines in economic growth, thereby further increasing economic inequality and potentially driving an additional 24 million people into extreme poverty by 2030. In the resulting report, the World Bank also highlighted that, by 2050, global increases in health-care costs could range from \$300 billion to more than \$1 trillion per year and a decline in global livestock production could range from 2.6 per cent to 7.5 per cent per year.

The World Bank suggests that addressing antimicrobial resistance should be considered one of the highest-yield development investments. It estimates \$9 billion in annual costs for antimicrobial resistance containment in low- and middle-income countries, with an economic rate of return ranging from 31 per cent to 88 per cent annually based on the proportion of costs avoided. The findings highlight that addressing antimicrobial resistance represents an excellent investment for countries⁷¹.

Strengthening public-private partnerships to promote research and development⁷²

In order to foster investment in new antimicrobials, as well as in safe and effective alternatives to antimicrobials for human, animal and plant health, the private sector, philanthropies and government institutions need to closely coordinate their efforts. The Tripartite Organizations (FAO-OIE-WHO) engage in ongoing dialogue with development partners and civil society organizations so as to support antimicrobial resistance initiatives within the broader sustainable

⁷¹drug-resistant Infections a Threat to Our Economic Future March 2017, © 2017 International Bank for Reconstruction and Development/The World Bank 1818 H Street NW, Washington, DC 20433

⁷²Follow-up to the political declaration of the high-level meeting of the General Assembly on antimicrobial resistance, 10 May 2019, A/73/869 agenda item 129

development agenda. One such initiative, a global antibiotic research and development partnership, jointly developed by WHO and the Drugs for Neglected Diseases initiative, is aimed at developing new treatments for bacterial infections. Through the partnership, WHO and the Drugs for Neglected Diseases initiative have launched programmes to address sepsis in newborns and to develop a new first-in-class treatment for drug-resistant gonorrhoea, which is entering the third phase of clinical trials.

Research priorities are embedded in WHO's action plans:

- WHO has published a list of 12 groups of pathogens (the global priority pathogens list), some of them causing common infections such as pneumonia or urinary tract infections that are increasingly resistant to existing antibiotics and urgently in need of new treatments; the aim is to guide and promote research and development.
- The Global Antibiotic Research and Development Partnership (GARDP) has been created to develop new antibiotic treatments addressing antimicrobial resistance, while ensuring equitable access for all in need. GARDP is being incubated by the Drugs for Neglected Diseases initiative (DNDi) in collaboration with the World Health Organization (WHO).
- Joint programming initiative on AMR (JPIAMR) has been set up to streamline the European research efforts in AMR by joint planning, implementation and evaluation of national research programmes; it coordinates annual joint calls for new research projects on AMR with EU or national funding.
- The Commission funds several antimicrobial resistance projects through its Health Programme and its research programmes.
- The development of cheap rapid diagnostic tests is also key to guide the appropriate use of antibiotics thereby reducing overuse and misuse.

In 2019, WHO issued a revised global priority list of antibiotic-resistant bacteria that pose the greatest threat to human health.

Sustainable access for health systems and patients is an essential & dynamic balance between stewardship, innovation and access. Developing new economic models to incentivise antibiotic discovery and development is the need of the hour despite knowing the disadvantages for putting R&D for antibiotics, as antibiotics are relatively cheap medicines with low return on investment. Initiatives that aim to explore new business models:

- “Push” incentives that support discovery and early phases of development: e.g. US government’s Biomedical Advanced Research and Development Authority (BARDA), JPIAMR, Wellcome Trust provide funding to the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), World Health Organization (WHO) and the Drugs for Neglected Diseases initiative (DNDi) have created the Global Antibiotic Research and Development Partnership (GARDP), supported by several European governments, the government of South Africa and the NGO Médecins Sans Frontières (MSF)
- “Pull” incentives that delink payment from prescribing volume and involves the promise of a reward for the development of new antimicrobials that target pathogens that represent a high AMR risk; eg, United States’ Generating Antibiotic Incentives Now (GAIN) Act- grants an additional five years of market exclusivity for companies developing antibiotics that target a selected group of qualifying pathogens.

- Platforms to discuss approaches, e.g. TATFAR, Duke-Margolis PAVE, DRIVE-AB, German Global Union for Antibiotics Research and Development (GUARD) Initiative and the UK Review on AMR.
- A European Union-based joint programming initiative on antimicrobial resistance has mapped the funding of research on antimicrobial resistance in relation to therapeutics, diagnostics, surveillance, transmission, the environment and interventions.
- The creation of a global antimicrobial resistance research and development hub by the Federal Ministry of Education and Research of Germany; the launch of the “Grand challenges” initiative of the Bill and Melinda Gates Foundation; the establishment of a research and development centre for antimicrobial resistance in the United Kingdom; the creation of an antibiotic development platform in the Netherlands; and the creation of a fund known as the “Replenishing and enabling the pipeline for anti-infective resistance impact fund”.

Because the development of new anti-bacterials may have fallen behind the rate of antibacterial obsolescence, incentives for new drug development are needed. Recent reports have suggested that government incentives are essential to encourage research and development (R&D) for novel anti-bacterials. New antibacterial drugs should fulfil three criteria: first, they should be drugs to which resistance has not developed and that do not exhibit cross-resistance with other drugs; second, they should have a narrow spectrum of activity to reduce the likelihood of resistance; and third, they should directly address public health needs. Possible financial incentives for antibacterial R&D include tax credits, advanced market commitments for purchase, payments for conservation, call options and orphan drug protection. It is also important that such incentives do not undermine efforts to preserve the effectiveness of existing drugs, and indeed, they could be targeted to promote such preservation. A tool for incentivization is transferable market exclusivity vouchers to re-enter the antimicrobial market. Rewarding the companies for their drug’s overall efficacy, and broader impact on global health, will not only allow them to profit enough but they will also want to invest in the initial research and development.

Importance of Multinational Coordination and Increased Public Financing for Antibiotic Innovation Significant financing is already occurring to bolster antibiotic innovation, including from a collaboration of 22 countries through the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR); Europe through its Innovative Medicines Initiative (IMI); the United States through its Biomedical Advanced Research and Development Authority (BARDA); the combined UK and US initiative, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X); the United Kingdom’s and China’s Global Innovation Fund; and the independent, not-for-profit Global Antibiotic Research and Development Partnership (GARDP). These initiatives are all vital sources of antibacterial innovation support. Yet none have protected, long-term financing, and the financing in total falls short of the estimated global need.

DRIVE–AB (i.e., Driving reinvestment in research and development for antibiotics and advocating their responsible use, www.drive-ab.eu), is a consortium of 16 public sector partners and 7 pharmaceutical companies supported by the Innovative Medicines Initiative (IMI) Joint Undertaking (www.imi.europa.eu), resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7/2007-2013) and

EFPIA (European Federation of Pharmaceutical Industries and Associations) companies' in kind contribution. DRIVE-AB is tasked with defining responsible use of antibiotics, identifying the antibiotic-related public health priorities, calculating the societal value of having new antibiotics available for these priorities, developing and costing new economic models to promote the desired antibiotic innovation, and sustainable use of the resulting, novel antibiotics. The purpose of the project is to transform the way policymakers stimulate antibiotic innovation and to ensure that these new antibiotics are used sustainably and available equitably⁷³.

The Interagency Coordination Group (IACG) on Antimicrobial Resistance was convened by the Secretary-General of the United Nations after the UN High-Level Meeting on Antimicrobial Resistance in 2016. The Secretariat for the IACG was provided by the WHO, with contributions from the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE). The IACG completed its mandate on 29 April 2019 upon the handover of its report to the Secretary-General⁷⁴.

CARB-X stands for Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator. It is non-profit global partnership funded by the United States government (through BARDA and NIAID, within the United States Department of Health and Human Services) and the Wellcome Trust, and has as its mission to invest US\$ 455 million in 2016-2021 to support the pre-clinical development of antibiotics and other therapeutics, rapid diagnostics, vaccines and devices to address the rise of drug resistance⁷⁵. Among its projects are eight new classes of antibiotics, many non-traditional therapeutics, projects to boost the body's microbiome, a vaccine, and four rapid diagnostics that will enable doctors to treat patients more quickly.

DRIVE-AB also recommended 'pull' funding – a big US\$ 1 billion market-entry reward for companies for each new antibiotic approved to attract more private investment antibacterial research. This prize would be in addition to any sales revenues. The G20, through its member countries, would be ideally positioned to take the lead globally on public funding of R&D and coordinating efforts to ensure a predictable supply of antibiotics over the next 30 years. The measures proposed by DRIVE-AB would cost an estimated US\$ 36 billion and produce some 20 new antibiotics over the next 30 years, which would go a long way to saving lives and battling the rise of superbugs.

GARDP ensures that R&D investment offers public health returns, delinking the cost of antibiotic treatments from the price of the products and volume-based sales through partnership, collaboration, and coordination as well as the adoption of innovative business models.

The goal is for effective antibiotic treatments to be made affordable and accessible to all in need and in a manner which minimizes the risk of inducing resistance.

GARDP's role within the global AMR R&D landscape

- Priority Target Product Profiles (TPPs): GARDP works with WHO to develop specific TPPs for key programmes
- Supporting the R&D ecosystem: GARDP helps build tools and resources that will support drug developers, especially in academia and small and medium-sized enterprises (SMEs) (e.g. see Exploratory/Upstream/Memory Recovery Programme)

⁷³Policy Brief The Importance of Multinational Coordination and Increased Public Financing for Antibiotic Innovation; DRIVE-AB: Transforming The Way Policymakers Stimulate Innovation, Responsible Use And Global Access Of Novel Antibiotics To Meet Public Health Needs (<http://drive-ab.eu/wp-content/uploads/2016/08/PolicyBrief-GovernanceFinance.pdf>)

⁷⁴<https://www.who.int/antimicrobial-resistance/interagency-coordination-group/en/>

⁷⁵<https://carb-x.org/>

- R&D implementation: GARDP will develop and execute programmes for key global health AMR priorities receiving insufficient investment (e.g. see Neonatal Sepsis Programme and Sexually Transmitted Infections Programme)
- Effective funding and partnering: GARDP will directly support and fund the work of developers, including SMEs, in developing new chemical entities (NCEs) of relevance through a direct partnership model
- Embedding access: Paramount to its model, GARDP will proactively work to ensure affordability, availability and stewardship according to public health needs are embedded within its R&D programmes from the outset

As an integral element of WHO's Global Action Plan on AMR GARDP is calling upon the global community to support its goal to develop and deliver five new treatments by 2025 - '5 BY 25' in response to the growing burden of antibiotic resistant infections. This will allow GARDP to bring five new treatments that address the most urgent public health needs to patients. The five new treatments will focus on the priority pathogens identified by WHO, and current unmet needs for diseases and key populations. This includes developing and delivering treatments for children, newborns with sepsis, and sexually-transmitted infections. Drug-resistant infections already cause at least 700,000 deaths globally each year⁷⁶.

The Consultative Expert Working Group (CEWG) on Research and Development had also highlighted open approaches to R&D and innovation, pooled funds, direct grants to companies, milestone prizes, end prizes and patent pools and the general principle of de-linking the costs of R&D from the price of the medicine, meaning that the investor does not have to recoup its R&D investment through the sales revenues. The report was also discussed by the WHO Member States in an open ended meeting in November 2012 and there was an agreement on a strategic work plan that included the creation of a WHO global health R&D observatory, implementation of a number of health R&D demonstration projects, and exploration of a potential financing mechanism for pooled contributions and coordination⁷⁷. In the case of developing countries, the market failure which intellectual property rights try to correct is compounded by a lack of reliable demand for the products generated by research and development. Thus the incentive offered by intellectual property rights fails to be effective in correcting the market failure.

Global AMR R&D Hub

The Global Antimicrobial Resistance (AMR) Research and Development (R&D) Hub was launched in May 2018, following a call from G20 Leaders to address challenges and improve coordination and collaboration in global AMR R&D using the One Health approach. The Global AMR R&D Hub will support global priority setting and evidence-based decision-making on the allocation of resources for AMR R&D through the identification of gaps, overlaps and potential for cross-sectoral collaboration and leveraging in AMR R&D. It will also promote coordination among governments in the fight against AMR. It is a global partnership currently consisting of 16 countries, the European Commission and two philanthropic foundations and four international organisations (as observers)⁷⁸. India, which is among countries with the highest bacterial disease burden in the world, has become a part of the Global Antimicrobial Resistance Research and Development Hub on September 12, 2019⁷⁹. With India as a member, the Hub now represents more than half the world's population. The Global AMR R&D Hub will seek to build on existing global initiatives and recommendations, avoid duplication of existing efforts and not act as a funding body itself.

⁷⁶<https://www.gardp.org/>

⁷⁷<https://www.who.int/phi/cewg/en/>

⁷⁸<https://www.gesundheitsforschung-bmbf.de/en/GlobalAMRHub.php>

⁷⁹<https://pib.gov.in/newsite/PrintRelease.aspx?relid=193143>

Though it arose from the G20, the Global AMR R&D Hub is open to non-G20 countries as well as nongovernmental donor organizations investing in AMR R&D.

The hub has a provisional work plan (2018-2021), under which it proposes to develop a dynamic dashboard, establish operational activities and operational procedures and engage experts in ad-hoc Expert Advisory Groups to understand the range of R&D incentives and gaps in the incentive toolbox. The dashboard will:

- Collect AMR R&D information (data) from human health, animal health, plant health and environmental health sectors (One Health);
- Capture as close to real time data from public and private (for profit and philanthropic) funded basic and applied R&D on therapeutics, preventives, diagnostics, policy, operational and implementation strategies and activities. R&D on therapeutics, preventives and diagnostics will be captured across the research and innovation value chain (from discovery to registration and application);
- Present high level data interactively;
- Allow high level comparison of R&D activities and funding across sectors; and
- Provide a platform that enables identification of gaps and duplications in AMR R&D activities, including incentives (both push and pull), to inform global research priority setting and to help accelerate innovation.

VI. Controlled Human Infection Model (CHIM) Studies-Regulatory and Ethical Considerations

Controlled human infection Model (CHIM) studies have a long and illustrious history of advancing the understanding of the pathogenesis, management and prevention of infectious diseases. The fundamental scientific value of being able to control the nature and timing of infection and interventions in well-characterised human subjects remains unchanged, but it is now greatly enhanced by advances in immunology, functional genomics, microbiomics, pharmacogenetics, pharmacokinetics and pharmacodynamics. CHIM studies have thus become a core methodology in modern infectious disease research⁸⁰.

Although CHIM studies have been performed since the pre-1940s, it is only in the last 10 to 15 years that the methodology has seen a resurgence, driven by the development of new therapeutics and vaccines against a range of organisms. This has in turn advanced the CHIM studies as a modern tool for attaining a deeper understanding of the pathogenesis of infection, as well as for drug and vaccine development. CHIM studies offer an efficient model for the selection of the most promising agents from a diversity of available candidates for further product development, and are increasingly being utilised to efficiently bridge safety and immunogenicity testing and phase II/III efficacy studies. CHIM studies not only allow efficacy data to be generated quickly, they also facilitate the identification of good immune correlates, the down-selection of vaccine candidates and early vaccine formulation decisions, thus avoiding unnecessary and costly large-scale trials.

University of Oxford has also designed, developed and done clinical evaluation of vaccines including those for meningococcal disease and enteric fever and leads studies using a human challenge model of (para)typhoid^{81,82}. University of Maryland School of Medicine, Center for Vaccine Development, Baltimore, USA has developed human infection challenge models for *Shigella*, diarrheagenic *E. coli*, and cholera to assess efficacy of new vaccine candidates.

In Europe and the United States (US), CHIM studies are regularly performed using various viruses, bacteria and parasites. Globally, the number of clinical trials conducted is on the rise and they are increasingly being conducted in less wealthy countries outside of the US and Europe, where the cost of running trials is substantially lower. CHIM studies, however, are still in infancy in Asian countries.

CHIM studies require a robust regulatory environment in order to ensure the safety of the infected subjects, protect the subjects' autonomy, and safeguard the staff and general public from onward transmission of infection from the study subjects.

Regulatory Considerations for CHIM Studies⁸³

The regulatory requirements for CHIM studies vary according to countries. The major difference lies in the requirements for the challenge pathogen. These include differences in

⁸⁰Balasingam S, Horby P, Wilder-Smith A. The potential for a controlled human infection platform in Singapore. *Singapore Med J* 2014; 55(9): 456-461 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4293939/pdf/SMJ-55-456.pdf>)

⁸¹Dobinson et al. Evaluation of the Clinical and Microbiological Response to *Salmonella* Paratyphi A Infection in the First Paratyphoid Human Challenge Model. *Clinical Infectious Diseases*; 2017;64(8):1066-73 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5439345/pdf/cix042.pdf>)

⁸²https://www.who.int/immunization/research/forums_and_initiatives/gvirf/Beth_Kirkpatrick_2018.pdf?ua=1

⁸³The Academy of Medical Sciences-Controlled Human Infection Model Studies: Summary of a workshop, 2018 (<https://acmedsci.ac.uk/file-download/55062331>)

the level of release testing required as well as the requirements set by the regulatory agency for the challenge pathogen to be deemed suitable for use before subjects are challenged in a clinical trial.

The regulatory requirements for CHIM studies vary according to countries. The major difference lies in the requirements for the challenge pathogen.

Global Regulatory Considerations for Human Challenge Studies

The regulatory requirements for CHIM studies vary according to countries. The major difference lies in the requirements for the challenge pathogen. These include differences in the level of release testing required as well as the requirements set by the regulatory agency for the challenge pathogen to be deemed suitable for use before subjects are challenged in a clinical trial.

For instance, FDA considers live organisms to be ‘biologics’ and has declared that an “Investigational New Drug Application (IND) is required for challenge studies in which live organisms (e.g., virus, bacteria, or fungi that is modified or wild-type) is administered to subjects to study the pathogenesis of disease or host response to the organism”. This is not, however, the position of the European Economic Area (EEA), which considers the challenge agent as a Non-Investigational Medicinal Product (NIMP). This means that it does not fall within the rules for manufacturing of medicinal products, as set out in Title IV of Directive 2001/83/EC⁵, or the rules for manufacturing of IMPs, as set out in Article 13 of Directive 2001/20/EC, Article 9 of Commission Directive 2005/28/EC and Commission Directive 2003/94/EC. While NIMPs do not have a marketing authorisation in the EU, they have to be manufactured under GMP guidelines, such that they are as safe for subjects as an IMP would be.

India Volunteer Research Infection Consortium (IVIRC) has been created and is evaluating India’s current thinking and position on Volunteer Infection (VI) studies, the long-term plan for VI studies in India, the extent of engagement and oversight for VI studies. The consortium will debate and discuss various aspects (laboratory, clinical research, clinical care, ethics, engagement etc.) of such studies and will develop way forward for CHIM studies in India⁸⁴. In the recently held 3rd Annual Regulators Conclave for Central and State Regulatory Authorities in India, jointly organized by CDSCO with WHO, Controlled Human Infection Model Studies was one of the sessions in the conclave. It was recommended that

- (i) A regulatory pathway guidance for Controlled Human Infection Model Studies in India needs to be developed by CDSCO, including ethical considerations with the support of THSTI, DBT, ICMR and WHO. A white paper in this regard may be prepared by THSTI and other stakeholders and shared with CDSCO.
- (ii) In India, human challenge trials could be considered as an innovative translational approach for certain public health solutions.

Role of WHO

One of WHO’s core functions is ‘setting norms and standards and promoting and monitoring their implementation’. WHO recommendations and guidelines are intended to ensure the availability of biological products of appropriate quality, safety and efficacy for use at a global level which also serve as benchmark for global acceptability of these products and as a basis for defining national regulatory requirements for licensing as well as for post-licensure evaluation. The work of IVIRC is supported by WHO along with national regulatory authority- India’s CDSCO and academia.

⁸⁴Expert consultation of India Volunteer Research Infection Consortium (IVIRC). Minutes of Meeting. New Delhi: Translational Health and Sciences Technology Institute; 2019

Typbar TCV® from Bharat Biotech - India, World's First Typhoid Conjugate Vaccine Prequalified by WHO⁸⁵

Bharat Biotech's Typbar TCV®, the world's first clinically proven Typhoid Conjugate Vaccine against typhoid fever has received prequalification from World Health Organisation (WHO). This enables the procurement and supplies of this life saving vaccine to UNICEF, Pan-American Health Organization (PAHO) and GAVI supported countries. Typbar TCV® is the first typhoid vaccine, clinically proven to be administered to children from 6 months of age to adults and confers long term protection against typhoid fever. Typbar TCV® has been evaluated in Human Challenge Studies at Oxford University and typhoid conjugate vaccines have been recommended by WHO's Strategic Advisory Group of Experts on Immunization (WHO-SAGE).

Typbar TCV® is a result of dedicated product development at Bharat Biotech since 2001, where all aspects of the product profile were studied and evaluated in human clinical trials. With 5 years of follow up data for seroconversion, Typbar TCV® at 25µg / dose has proven long term protection for children and adults alike, and can be administered to children from 6 months of age.

Oxford University conducted a human challenge study with Typbar TCV® at 25µg / dose, where the subjects were challenged with live *S. said* Prof Andrew Pollard, University of Oxford.

Bharat Biotech is able to supply up to 50 million doses / year and is actively working on expanding its manufacturing capacity to reach ~ 200 million doses. This will truly fulfill its mission to develop novel vaccines, manufacture and supply high volumes of high quality vaccines at affordable prices for low income countries and low-middle income countries.

The perspective of the international counterparts, pioneer in this field will be of great value to lead the way for CHIM studies in India.

There is also a discussion of having a cross regional collaborative guidance on CHIM Studies, with WHO South East Asia Regional Office (SEARO) and also acknowledging the functioning of South-East Asia Regulatory Network (SEARN). There is interest in understanding whether a regional group of regulators and SEARN can develop regulatory guidance. AVAREF (African regulatory network) had been looking into this as several countries in WHO AFRO are conducting volunteer infections studies. More recently, Department of Biotechnology (DBT), Government of India has launched an India-EU Influenza call with a requirement for volunteer infection studies. A side meeting has been organized on CHIM Studies for global experts' thinking on the issue and to discuss the contours of the cross regional guidance and leverage South-East Asia Regulatory Network (SEARN) for the same.

⁸⁵WHO prequalified Typhoid vaccine, 2018 (<https://www.who.int/medicines/news/2017/Bharat-Biotech-TypbarTCV-WHO-PQ-Press-Release-Global-Final.pdf>)

VII. Health Technology Assessment as a Tool for Evidence Based Decision Making in Healthcare

Health technology assessment (HTA) refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology. The main purpose of conducting an assessment is to inform a policy decision making. Considering the definition of health technology, as the application of organized knowledge and skills in the form of medicines, medical devices, vaccines, procedures and systems developed to solve a health problem and improve quality of life⁸⁶.

Health technology assessment (HTA) is a multidisciplinary process that gathers policy relevant evidence about the medical, social, economic and ethical issues related to the use of a health intervention in a systematic, inclusive, transparent and robust manner. Health Technology Assessment was initiated 30 years ago in World Health Organization and two regional offices (EURO and AMRO), considering HTA a way to strengthen evidence based selection and rational use of health technologies and increase efficiency when introducing and using these technologies in health care. Subsequent WHO Resolutions indicate that HTA is a tool to further advance the implementation of Universal Health Coverage (UHC) in terms of deciding getting right intervention at lowest possible cost. These concepts are linked to people centered care, essential packages, resource allocation, and most important, quality of health services delivery to get more cost-effective healthcare⁸⁷.

The rapid emergence of new and expensive drugs, devices, technologies, diagnostics etc. coupled with the growing public expectation for accessing such treatments at an affordable level has led to the pressure of delivering high quality healthcare with constrained public funds in developing countries. These conditions heighten the importance of evidence – based decision making for resource allocation and strategic planning of policymakers and other key stakeholders. For these decisions, Health Technology Assessment (HTA) has emerged as an important tool to inform allocation and decisions within limited resources⁸⁸.

Universal Health Coverage aims to provide quality healthcare at minimum cost to the people. This is key to accelerating country progress towards better health is to provide accessible and affordable medical health services to each communities and State.



Source: <http://www.somalilandsun.com/>

⁸⁶https://www.who.int/medical_devices/assessment/en/

⁸⁷Prinja S, Chauhan AS, Angell B, Gupta I, Jan S. A systematic review of the State of Economic Evaluation for Health Care in India; Health Economic Health Policy -2015 Dec;13(6):595-613.

⁸⁸Prinja, S., Downey, L. E., Gauba, V. K., & Swaminathan, S. (2018). Health technology assessment for policy making in india: current scenario and way forward.

Health Technology Intervention Assessment (HITA) in the Department of Health Research (DHR) in India

In recent years, a national Health Technology Intervention Assessment (HITA) body, the HTAIIn, has been set up in the Department of Health Research (DHR), Ministry of Health and Family Welfare, Government of India to develop and coordinate HTA activities in the country. The main aim of the HTA program in India is to engage in explicit and evidence-based priority setting of health resources towards providing universal health coverage for all individuals. In October-2018, Government of India also launched a Manual on Health Technology Assessment for all health professionals to facilitate the process of transparent and evidence informed decision making in the field of health. The manual lays down the various approaches to HTA, dealing with safety, efficacy/effectiveness, economic, organizational, ethics, social and legal aspects. This is a landmark step towards efficient and effective implementation through evidence based decision making in the healthcare system. This structure that is both comprehensive and inclusive defines HTAIIn⁸⁹.

The Health Technology Assessment Compendium was launched jointly by WHO India and National Health Systems Resource Centre (NHSRC), Government of India in 2012-13 as an outcome of this HTA fellowship program. This First Compendium of HTA highlights the most essential health technologies required today for responding to India disease burden.

The activities of HTAIIn are:

- To support the process of decision making in healthcare at the Central and State policy level by providing reliable information based on scientific evidence.
- Develop Systems and mechanisms to assess new and existing health technologies by transparent and inclusive processes.
- To collect and analyze evidence in a systemic and reproducible way and ensure its accessibility and usefulness to inform health policy.
- Disseminate research findings and resulting policy decisions to educate and empower the public to make better informed decisions for health.

The operational objectives of HTAIIn are:

- To inform Government health department officials about clinical and cost effectiveness of any intervention to be undertaken in public health programs.
- To inform research agencies about evidence gaps and health research requirements to support policy.
- Informing hospitals and other health care organizations to help in decisions regarding technology acquisition and management.
- To inform clinicians and patients about the appropriate use of health care interventions for specific clinical needs and circumstances.

The Government of India is committed to extend healthcare services to its 1.3 billion population as part of India's Universal Health Coverage agenda. Given the constraints in resources, it is a challenge for the government to devise ways to reduce catastrophic health expenditure and ensure affordable access to essential health care for the entire population⁹⁰.

The magnitude of the problem can be estimated from the fact that in 2014-15 National Health Accounts Estimates for India reported that the out-of-pocket expenses spending on health by households was 62.6% of the total health expenditure of the households which was high as 2.4% of total GDP per capita. The Healthcare policy decisions are based on latest and clinically proven evidence. In India this may not be an easy task- because India specific evidence is limited.

⁸⁹<https://dhr.gov.in/about-mtab>

⁹⁰Country case studies provide useful lessons to achieve and sustain universal health coverage

Two main types of evidence that are required to perform a health technology assessment are clinical effectiveness, which provides information on the clinical benefit and safety of health technologies and cost-effectiveness, which helps to answer the question.

Evidence on Clinical effectiveness

The type of clinical effectiveness depends on the type of health technology being appraised but it can be defined as the measure of effect on the course of the relevant disease of interest. Evidence on treatment effect and safety of health technologies is commonly derived using experimental or observational study design.

Evidence on Cost-effectiveness

Health economic evaluations are a critical part of health technology appraisals. Decision –analytic models follow a systemic approach in bringing together evidence on clinical effectiveness, outcomes measured as changes in natural units of disease specific measures or in health-related quality of life and cost associated with a health technology relative to another.

The various Health Technology Assessment regional centres of India:

1. Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh
2. Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Kerala
3. National Institute for Research in Tuberculosis (NIRT), Chennai
4. Regional Medical Research Centre (RMRC), Bhubaneswar
5. Indian Institute of Public Health (IIPH), Shillong
6. Kalam Institute of Health Technology, Vizag
7. National Health Systems Resource Centre, Delhi

The Studies of Health Technology Assessment assigned to resource hubs in India under Department of Health Research, Government of India:

1. HTA of Intra Ocular Lenses for treatment of age-related Cataract Surgery in India
2. HTA of Cost effectiveness of Safety Engineered Syringes for Therapeutic use in India (implemented)
3. HTA of Strategies for Cervical Cancer Screening in India
4. HTA for Screening of Type 2 Diabetes and Hypertension in India (PGIMER)
5. HTA for Breast Cancer Screening in India (NHSRC)
6. HTA of Long Acting Reversible Contraceptives in India
7. HTA of Uterine balloon tamponades to manage postpartum haemorrhage in India

The drive to achieve Universal Health Coverage raises the need to choose and manage effective technologies that are to be adopted within countries' health systems, particularly in a context of limited resources. Developing and strengthening national capacity will have to build on established best practices, information exchange and collaborative approaches to make the best use of limited resources and yield robust scientific assessments⁹¹.

The information produced by health technology assessment (HTA) can be used to enhance decisions about the use and diffusion of technology⁹². The success or otherwise of HTA needs to be addressed primarily in terms of the downstream impact on health outcomes and the performance of health systems⁹³.

Health technology assessment provides the basis for evidence-based priority setting and policy decisions. This aims to maximize access to quality healthcare at minimum cost to the people of the country⁹⁴.

⁹¹www.oecd.org/health/health-systems/briefing-note-chile

⁹²<http://www.oecd.org/sti/emerging-tech/healthtechnologiesanddecisionmaking.htm>

⁹³Health Technologies and Decision making – ISBN-92-64-01620-i-©OECD 2005

⁹⁴Fox-Rushby J, Cairns J. Economic evaluation, London: Oxford University Press;2006

VIII. Leveraging Regulatory Networks for Access to Quality, Safe and Affordable Medical Products Including Digital Tools for Strengthening Regulatory Systems

Access to quality medical products is crucial for achieving universal health coverage (UHC) and in reaching the SDGs for health. Regulators face a number of challenges today and these are related to the wide variety of medical products that they have to deal with (medicines, vaccines, diagnostics and medical devices). In this context, there is need of a new strategic regulatory approach to ensure product safety, efficacy, and quality.

Greater harmonization, coordination and alignment of regulatory rules across nations would be beneficial for better public health outcomes and increase access to safe, effective and quality medical products. Regulatory authorities are working more frequently with each other, sharing inspection and safety information, and even conferring over discrete product approvals. Various bilateral and multilateral arrangements seek to enhance collaboration, learning, and sharing of best practices as well as efforts to strengthen the regulatory science that underlies regulation and oversight.

A regulatory network provides a platform for communication and enabling cooperation and support to the national regulatory authority (NRA) of each country for quality and safety efficacy of medical products in a timely and efficient manner.

South-East Asia Regulatory Network (SEARN)

WHO South-East Asia Region (SEAR) member states launched the South-East Asia Regulatory Network (SEARN) to enhance information sharing, collaboration and convergence of medical product regulatory practices across the Region to guarantee access to high-quality medical products. The SEARN includes 11 Member States: Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste. The Key identified priority areas for SEARN are (1) Quality assurance and standards of medical products, including labs (2) Good regulatory practices including GMP, GDP etc (3) Vigilance for medical products and (4) Information sharing platform and (5) Medical device and Diagnostics⁹⁵.

The Network is taking forward the aspirations of Member states in line with, Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA), World Health Assembly Resolution WHA61.21, "Regulatory system strengthening for medical products", WHA67.20 and the South-East Asia Regional resolutions SEA/RC59/R9 on International Trade and Health, SEA/RC62/R6 measures to ensure access to safe, efficacious, quality and affordable medical products, and SEA/RC66/R7 on effective management of medicines. SEARN aims to promote efficiencies and enable availability of affordable and quality medical products through collaboration and reliance among regulators which will help to address challenges emerging due to country specific standards/review procedures.



⁹⁵<http://www.searo.who.int/entity/medicines/regulation/Tab-1/en/>

The SEARN Information sharing platform (ISP) Gateway was highlighted in the Access to medical products roundtable in the Ministerial Conference in 2018 Regional Committee⁹⁶.



The Delhi Declaration 2018 “Improving access to essential medical products in the South-East Asia Region and beyond” encouraged Member states to “Continue the momentum to strengthen regulatory cooperation and collaboration to improve the availability, quality and safety of essential medical products through SEARN”⁹⁷. The SEARN ISP has made publicly available information of all the 11 State Drug Regulators in SEARO accessible through a single ISP Gateway. As a principle, the Information Sharing Platform (ISP) relies on existing internet resources and web links to avoid duplication of efforts by the National Regulatory Authorities (NRAs). Another advantage of using existing country resources on the web is that the information on the Webpages of the NRAs is usually up to date and gives the current information. By linking up with existing information systems a time lag will be avoided and the latest documents will be available to SEARN members.

PAN America Health Organization⁹⁸

Created with the financial support of the United States, Brazil, and Canada, and with PAHO acting as Secretariat in charge of its development, The Pan American Network for Drug Regulatory Harmonization (PANDRH) is an initiative of the national regulatory authorities within the Region and the objective of Pan American Network for Drug Regulatory Harmonization (PANDRH). The regulatory exchange platform (REPs) was launched as a digital tool to support the secure exchange of non-public information between regulatory authorities in the Americas and elsewhere. The platform seeks to improve the exchange of information, streamline the use of resources, and promote regulatory harmonization and convergence in the Region

- Strengthen the regulatory functions and systems of the countries of the Region
- Develop, approve and implement common proposals taking into account international guidelines and standards for regulatory convergence
- Develop core competencies aimed at supporting and strengthening good regulatory practices and regulatory science in the Member States.

European medicines regulatory network⁹⁹

The system for regulating medicines in Europe is based on a closely-coordinated regulatory network of national competent authorities in the Member States of the European Economic Area (EEA) working together with the European Medicines Agency (EMA) and the European Commission. The European medicines regulatory network coordinates and supports interactions between over fifty national competent authorities for both human and veterinary medicines. These national authorities supply thousands of European experts to take part in

⁹⁶<https://searn-isp.org/SEARN/en/Home>

⁹⁷<http://www.searo.who.int/mediacentre/releases/2019/global-health-leaders-adopt-delhi-declaration-on-digital-health/en/>

⁹⁸https://www.paho.org/hq/index.php?option=com_content&view=article&id=12206:pjph-efforts-to-improve-regulation-of-medicines-in-the-americas&Itemid=135&lang=en

⁹⁹<https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network>

EMA's scientific committees, working parties and other groups. The regulatory network also includes the European Commission, whose principal role in the European system is to take binding decisions based on the scientific recommendations delivered by EMA.

By working closely together, this network ensures that safe, effective and high-quality medicines are authorized throughout the European Union (EU), and that patient, healthcare professionals and citizens are provided with adequate and consistent information about medicines.

The Benefits of the network for EU citizens –

- Enables Member States to pool resources and coordinate work to regulate medicines efficiently and effectively
- Creates certainty for patients, healthcare professionals, industry and governments by ensuring consistent standards and use of best available expertise
- Reduces the administrative burden through the centralised authorisation procedure, helping medicines to reach patients faster
- Accelerates the exchange of information on important issues, such as the safety of medicines

EMA and the national authorities depend on standards, processes and Information Technology (IT) systems that allow important information on medicines to be shared between European countries and analysed together. Some of the data are supplied by the Member States and centrally managed by EMA. This supports an exchange of information on a number of issues, including suspected side effects reported with medicines; the oversight of clinical trials and the inspections to check compliance with good practice in the clinical development, manufacturing and distribution, and safety monitoring of medicines. This helps to reduce duplication and supports efficient and effective regulation of medicines across the EU.

The African Vaccine Regulatory Forum (AVAREF)

The African Vaccine Regulatory Forum (AVAREF) is a regional regulatory network founded by WHO, focus on clinical trials of vaccines began to shift from developed countries to developing countries, including those in sub-Saharan Africa. The network brings together national regulatory authorities (NRAs) and ethics committees of the countries in the WHO African Region. It currently has 23 members. AVAREF promotes convergence towards harmonization of regulatory practices and processes to ensure timely regulatory evaluations and approvals of clinical trial applications and products¹⁰⁰.

Key among AVAREF's achievements has been firstly the establishment of innovative regulatory pathways for clinical trials, secondly the development and use of common guidelines for submission of clinical trial applications, and thirdly the use of joint reviews of multi-country clinical trial applications and joint good clinical practice (GCP) inspections. AVAREF is a WHO-supported platform that has proven to be instrumental in providing regulatory support to accelerate product development during public health emergencies, as exemplified with products in development against Ebola, these achievements will also support the work of African regulators on vaccines for diseases such as HIV, tuberculosis and malaria, which are affecting many millions of people in the African region. Lastly, AVAREF may serve as an important regional platform linked with international networks such as the Developing Countries Vaccine Regulatory Network (DCVRN) to promote the increasing number of multi-regional or global trials.

¹⁰⁰<https://www.afro.who.int/>

The African Medicines Regulatory Harmonization Program is a partnership initiative formalized in 2009 and launched throughout the East African community in 2012 (Tanzania, Uganda, Kenya, Burundi, Rwanda). This program was created through a joint initiative of the New Partnership for Africa's Development (NEPAD), the Pan African Parliament (PAP), and the African Union Commission (AUC), in collaboration with the World Health Organization (WHO), the World Bank, the Bill & Melinda Gates Foundation (BMGF), and the United Kingdom's Department for International Development (DFID). The main objective of the AMRH program is to create regulatory mechanisms that are effective, efficient and transparent to achieve faster approval and subsequent availability of the products in various African markets. The strategy of this program is to develop regional regulatory platforms with harmonized standards (technical requirements/guidelines), joint regional dossier assessments and Good Manufacturing Practice (GMP) inspections, including work-sharing and streamlined decision making processes. NEPAD Agency (a technical body of the African Union) and the AUC defined and endorsed the regional networks for implementation of the AMRH program.

There is a need for shortened, predictable and more transparent regulatory pathways and marketing authorization procedures to avoid delayed access to needed medical technologies. The need to simplify regulation while maintaining its stringency and cost-effectiveness requires more coordination through regional and international regulatory mechanisms.

Within the framework of the EAC-MRH project, medicines are authorized through one of three channels: The National Authorization Procedure, the WHO Collaborative Procedure and the EAC Joint Assessment Procedure. Under the National Authorization Procedure, each EAC Member State has its own procedures for the authorization of medicines. However, each uses the EAC harmonized guidelines for registration of medicines. This procedure will yield marketing authorization in EAC Member State(s) where the application was submitted. The WHO Collaborative procedure is collaboration between the WHO Prequalification of Medicines Program (WHO/PQP) and interested NMRAs. This procedure can be used for the assessment and accelerated national registration of WHO prequalified pharmaceutical products. Applicants interested in registration in two or more EAC Member States can submit product registration dossiers through the EAC Joint Assessment Procedure. This procedure entails joint assessment of selected medicinal products and joint inspection of their respective manufacturing site(s) by designated assessors.

International Conference of Drug Regulatory Authorities (ICDRA)

WHO has been playing a vital role in terms of improving regulation to provide a platform for regulators to discuss common challenge and identify areas where further guidance for regulators need to be developed. The WHO has convened the International conference of drug regulatory authorities (ICDRA) every 2 years since 1980 with the aim of promoting exchange of information and collaborative approaches to issues of common concern¹⁰¹. The ICDRAs have been instrumental in guiding regulatory authorities, WHO and interested stakeholders and in determining priorities for action in national and international regulation of medicines, vaccines, biomedicines and herbals. As a platform established to develop international consensus, the



¹⁰¹https://www.who.int/medicines/areas/quality_safety/regulation_legislation/icdra/en/

ICDRA continues to be an important tool for WHO and drug regulatory authorities in their efforts to harmonize regulation and improve the safety, efficacy and quality of medicines. The 19th International Conference of Drug Regulatory Authorities (ICDRA). 2020 ICDRA will be hosted in New Delhi, India from 28th September- 2nd October 2020.

A progressive regulatory system in India

The Government of India has shown commitment and strong political will to strengthen and build capacity of national regulatory authorities. More than USD 240 million (1700 Crores) have been approved by the Union Cabinet for strengthening the Indian drug regulatory system. The major components are the human resources. In the cabinet note, there is additional creation of 1000 posts for the Central Drugs Standard Control Organisation (CDSCO) and 2500 additional post for the states. There is a provision for establishment of 6 new labs for CDSCO; and for e-governance which is already implemented. There is also a provision for National Drug Regulatory Academy, for time being started at the National Institute of Biologicals (NIB), Noida and 8 mini labs at the different port offices.

CDSCO has been assessed as per WHO global bench marking tool for vaccines and has been declared “functional’ with a maturity level of 4, i.e., the highest level as per currently evolved definitions in respect of 5 functions, and maturity level 3 in respect of 4 functions. While maturity level 4 indicates good results and sustained improvement trends, maturity level 3 reflects systematic process based approach, early stage of systematic improvements, data availability regarding conformance to objectives and existence of improvement trends.

In India, Ministry of Health and Family Welfare, Government of India is responsible for laying down the standards and ensuring safety, efficacy & quality for Drugs and implementation of e-Governance at CDSCO through SUGAM portal has brought simplicity, transparency, reliability, accountability, and timeliness and also simplified ease of business. The e-governance portal (SUGAM portal) has been set up to provide a “single window” for multiple stakeholders (Pharma



Industry, Regulators, Citizens) involved in the processes of Central Drugs Standards Control Organization, “SUGAM” enables online submission of applications, their tracking, processing & grant of approvals online mainly for drugs, clinical trials, ethics committee, medical devices, vaccines and cosmetics. The objective of the Sugam project is to consolidate the Indian Drug Regulatory Framework by streamlining the CDSCO processes, to enable paperless grant of various clearances by CDSCO and to enable higher level of transparency in Drug regulatory processes.¹⁰²

As part of E-Governance initiatives, CDSCO and CDAC have implemented SUGAM Labs which has been developed recently for the drug testing laboratories (www.sugamlabs.gov.in). The software integrates the different CDTLs and RDTLs through common portal. The software built

¹⁰²https://www.cdac.in/index.aspx?id=st_egov_sugam_ad

in comprehensive provisions for managing sampling points, receive samples, allocate storage location & manage custody, manage samples, tests, specifications, MDL, formula, sample registration including pre-register, register, allot, tests, barcode samples, publishing of test results subject to release with 2 levels of review and approval and configurable approval workflows for different sample types with Built-in audit trail, access to instrument data, inventory usage, comments, re-tests from traceability prospective. The SUGAM Labs software application can be extended to all the State Drug Testing Laboratories with the approval of the competent authority and urged all the States to utilize this facility. The e-governance portal (SUGAM portal) set up at the Central Regulatory Authority is being linked to the state regulatory authorities. The Central Government has amended the Drugs and Cosmetics Rules, vide G.S.R.19 (E) dated 10.01.2019 making online submission of data through SUGAM portal as a mandatory requirement under the Rules to create a comprehensive data base of the manufacturing licenses and drug products¹⁰³.

¹⁰³https://www.who.int/medicines/areas/quality_safety/regulation_legislation/icdra/ICDRA2020/en/

IX. Smart Safety Surveillance for Strengthening Pharmacovigilance Systems

There is an evolving product landscape with new vaccines, drugs, and diagnostics that are made by multiple manufacturers in different geographies. Many of these products are specifically developed for countries that have a unique disease burden, so use of these products and consequent post-marketing safety surveillance cannot rely on developed economies alone.

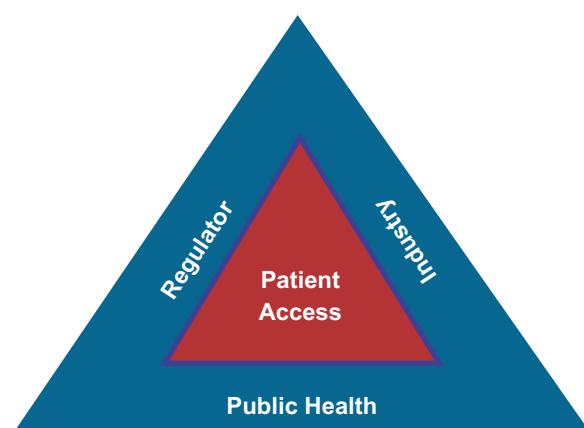
Post-marketing safety surveillance is essential for global health treatment and immunization programmes because all risks and benefits of a drug or vaccine are unknown at the time of approval. Under real world conditions, without timely and accurate information on safety and effectiveness particularly in resource poor settings, poor quality products can unnecessarily harm patients.

The Smart Safety Surveillance (Triple S) Programme is a collaborative effort among regulators, the national immunization programme in India and other key vigilance stakeholders for vaccines, to strengthen pharmacovigilance (PV) capacity. WHO has promoted the Smart Safety Surveillance (3S) approach with the support of Bill and Melinda Gates Foundation, to strengthen PV systems in developing countries that are introducing new health products, for the safe and effective use of these products. Rotavac, an oral rotavirus vaccine developed, tested and licensed in India, and introduced into the national immunization programme in 2016 for the prevention of rotavirus diarrhoea in young children, was selected as the vaccine pathfinder, to introduce and test the 3S approach.

The approach was achieved by implementing Smart Safety Surveillance systems for Rotavac vaccine in India by:

- I. Strengthening the functionality of current Pharmacovigilance systems
- II. Building capacity to analyses safety data
- III. Improving capacity to use Pharmacovigilance data for regulatory decision-making
- IV. Supporting the collaboration between public health programmes, academic researchers conducting Pharmacovigilance studies and regulators.

Smart Safety Surveillance: Mission Statement:
Robust, real-time evidence for best informed public health decisions



Every person deserves the right to have safe medical products

¹⁰⁴https://www.who.int/medicines/regulation/medicines-safety/publications/ACSoMP_14.pdf

Project 3-S: Smart Safety Surveillance in India

The activities to drive the Smart Safety Surveillance programme were undertaken in 2019 in India focusing on strengthening the collaboration of key stakeholders on vigilance. Specific workshops were conducted for Periodic Safety Update Report (PSUR) and Risk Management Plan (RMP) assessment, successful writing of Periodic Safety Update Reports (PSUR) and Risk Management Plans (RMP), Signal Detection Management, and Risk Benefit Assessment for vaccines.

There were two study visits organised to MHRA, UK and EMA, Amsterdam to understand the best practices of the risk benefit assessment and vigilance processes at MHRA and EMA. These culminated into collaborative workplans for hand-holding among the agencies in the coming years for strengthening capacity in vigilance. WHO, in collaboration with the Medicines Healthcare Products Regulatory Agency (MHRA) worked with the immunization programme, Ministry of Health and Family Welfare of India (MoHFW) and Central Drugs Standard Control Organization (CDSCO) to form a PV strengthening work plan for vaccines. The 3S focus in India was to link PV activities between different stakeholders, for data sharing, signal detection, risk assessment, risk management, risk communication, and benefit harm evaluation for regulatory decision making.

There are several learnings from the smart safety activities implemented in India, which directly lead to required next steps, including the need for collating safety data from all sources for safety assessment of the vaccines in the post marketing period including routine data collection and special studies.

As part of the Smart Safety Surveillance for vaccines, India focussed on the newly introduced Rotavirus vaccines and has available safety data from various sources. As part of special safety/impact studies, data are being collected at various sites including sentinel sites such as Adverse event following immunization (AEFI) Secretariat (Immunization Division) Ministry of Health and Family Welfare, Translational Health Sciences & Technology Institute (Department of Biotechnology, Ministry of Science & Technology), INCLEN, Centre for Health Research and Development, Society for Applied Studies, among others. In addition, the Central Drugs Standard Control Organization (CDSCO) is receiving safety reporting data periodically as PSURs. The PVPI also collects the vaccine AEFIs through E2B reporting by manufacturers, which is further shared with the Immunization Division. It was agreed that as the next steps, a team of experts from AEFI



Secretariat Immunization Division, CDSCO and sentinel sites such as THSTI, INCLEN, SAS and WHO Country Office for India would undertake the analysis of data received from all sources for AEFIs for Rotavac vaccines in India. The collated data would be analysed and a white paper on Rotavac safety would be jointly prepared. This white paper is to be released during the 2019 World Conference on Access to Medical Products, the flagship annual world conference of Ministry of Health & Family Welfare with WHO, and supported by partners (THSTI, BIRAC, ICMR).

Patient safety is a fundamental principle of health care. Delivering safer care and preventing harm, particularly “avoidable harm”, is one of the greatest challenges in today’s complex, pressurized and fast-moving environments. As a next step, Smart Safety Surveillance activities will be expanded to other levels of the health system in line with the national scale-up plan for pharmacovigilance in India. It is hoped that this approach leads to better characterized safety profile of Rotavirus vaccines and enhanced pharmacovigilance systems that support regulatory decisions for all vaccines throughout their lifecycle.

Project 3-S: Smart Safety Surveillance-Africa

The ultimate goal of Project 3-S is to establish end-to-end pharmacovigilance systems, with timely and adequate reporting of adverse drug reactions, followed by timely review and any needed regulatory action. A holistic plan for pharmacovigilance will be developed in each country, covering: (1) Policy, law and regulation, (2) system, structure and stakeholder coordination, (3) signal generation and data management, (4) risk assessment and evaluation, and (5) risk management, communication and allocation of commensurate resources. Project 3-S will serve as a pathfinder pilot for this approach in the area of pharmacovigilance. Work sharing and joint activities in ongoing initiatives such as the African Medicines Regulatory Harmonization (AMRH) and the African Vaccines Regulatory Forum (AVAREF) could create significant synergy and enhance impact. For example, a product could be monitored intensively in one or two countries and the data made available to neighbouring countries, or regional risk assessment committees could jointly review data on priority products for mutual learning and regional decisions.

X. Moving Towards Smarter Clinical Trials – Changing the Paradigm in the Context of Global and Multi-Regional Clinical Trials

Drug development has been globalized, and multi-regional clinical trials (MRCT) for regulatory submission has widely been conducted by many discovery based global pharmaceutical companies with the objective of reducing the time lag of launch in key markets and improve patient access to new and innovative treatments. Sponsors are facing several challenges while conducting multi-regional clinical trials. Challenges under the various topics of statistics, clinical, regulatory operational, and ethics have been discussed.

The challenges with many clinical trials including inadequate study design, insufficient power to answer the study question, lack of specificity and/or fidelity to the trial protocol, and incomplete reporting of outcomes and adverse events. There is a need to evaluate trials prior to initiation, with a specific focus on design, analysis, reporting, and feasibility. The three steps to help advance these goals: (1) Conduct landscape analyses to determine how any new study would fit into the world of ongoing/existing studies, (2) ensure independent third-party scientific review, and (3) ensure complete trial registration and results reporting.

In the context of capacity building, focused on training regulators on International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines for Good Clinical Practice (GCP) and Multi-Regional Clinical Trials (MRCT). The MRCT Center has been endorsed as Training Partner by ICH and as Training Center of Excellence by the Asia-Pacific Economic Cooperation (APEC). Starting in 2019, the MRCT Center has begun conducting in-country training, two of which have been held in collaboration with Health Canada in Ottawa Canada in February 2019 and at MRCT Centre of Brigham and Women's Hospital, USA in April, 2019.

Challenges of harmonization in the design and planning of MRCT

Regulators in different countries such as USA, EU-Japan, and China have issued guidance documents in respect of MRCT's. Lack of harmonization in the design and planning of MRCT is perceived to create a difficult situation to sponsors adversely affecting progressing MRCT in more and more discoveries. ICH E5 guideline was adopted in 1998 (updated in 2006) with the purpose to facilitate the registration of medicinal products among different geographic regions by recommending a framework for evaluating the impact of ethnic factors upon the efficacy or safety of a product. To address the challenges faced by Regulatory agencies and promote conducting MRCT by sponsors, a harmonized international guideline especially focusing on scientific issues in planning, designing MRCTs, International conference on harmonization (ICH) has developed ICH E17. This new guideline complement the guidance on MRCTs provided in ICH E5 and facilitate MRCT data acceptance by multiple regulatory agencies¹⁰⁵. The ICH E17 guideline defines the factors that must be considered in planning, designing, and executing MRCTs. MRCTs can facilitate simultaneous global development of a drug and reduce the number of clinical studies conducted separately in each region, thereby minimizing unnecessary duplication of studies. Although MRCTs require more coordination during the

¹⁰⁵<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4840793/>

planning stage and possibly increase start-up time, their use may provide a pathway for earlier ICH E17 Guideline access to new drugs worldwide by facilitating earlier approval across regions, thereby avoiding significant lag in the availability of new drugs in some regions.¹⁰⁶

The MRCT Center is a research and policy center associated with two of the world's most respected names in healthcare and academia: Brigham and Women's Hospital and Harvard University. Multi-Regional Clinical Trial: The mission of the MRCT Center was defined as to focus on the design, conduct and oversight of multi-regional clinical trials with an emphasis on those issues involving the emerging economies.

The MRCT Center has four primary areas of focus that address pressing issues in multi-regional clinical trials.

- Identify regulatory, oversight, and ethics issues and facilitate solutions in clinical trials around the world
- Resolve regulatory and ethical issues in order to improve the clinical trial enterprise
- Foster respect for clinical trial participants by working to improve the ethics, safety and transparency of clinical trials
- Promote regulatory convergence within multiple regions to accelerate innovation and improve health care around the world

Sponsors of MRCTs are encouraged to have scientific consultation meetings with relevant regulatory authorities. These interactions should take place during the planning stage of MRCTs to discuss the regulatory requirements for the overall development plan and the acceptability of MRCT data to support marketing authorizations. Conducting such consultation meetings early in the planning stage of MRCTs will enable the comments received from regulatory authorities to be taken into consideration. Inter-authority scientific discussions are encouraged to allow for harmonization of study requirements MRCTs can expedite global clinical development and facilitate registration in all regions across the globe. The ultimate goal of MRCT is to bring new medicines to patients globally as fast as scientifically possible and reduce the drug lag. MRCT also helps in expansion of clinical research into developing countries bringing medical care options to subjects who otherwise may not have access to them. Investment in drug development increases potential benefits to local scientific and medical and paramedical professionals. It provides access to more advanced technologies and helps in the development of technical expertise. MRCT provides the sponsors access to otherwise untapped pools of patients, as well as early patient access to new medications.



Different national health authorities are also supporting guidance for MRCTs. The Pharmaceuticals and Medical Devices Agency (PMDA) in Japan has made concerted effort for standardization so that more and more MRCTs are conducted in the country and drug lag is reduced. The Chinese FDA also issued guidance on MRCTs of drugs in early 2015, to see more trials happening in the country. Other collaborations exist among APAC countries. China, Japan, and South Korea's Tripartite Cooperation on Clinical Research aims to improve the landscape of clinical trials among the three countries because they are believed to have similar genetic homogeneity and disease patterns. Trial data generated in South Korea and China have frequently been accepted for drug registration in Japan. Harmonization agreements also are in place between Taiwan and Japan; and between

¹⁰⁶<https://www.ich.org/products/guidelines/efficacy/efficacy-single/article/general-principle-on-planningdesigning-multi-regional-clinical-trials.html>

Taiwan and APEC (Asia-Pacific Economic Cooperation) organization to support clinical trials and easier goods exchange.¹⁰⁷ Several harmonization initiatives exist between Asian countries to support easy data acceptability and reduce drug approval timelines in the region. ASEAN countries' harmonization initiative has standardized the drug approval process with common documentations, ASEAN Common Technical Documents (ACTD) and ASEAN Common Technical Requirements (ACTR). ACTD gives information on the format and structure of the dossier to be used for applications in the ASEAN region, while ACTR is a set of written material intended to guide applicants to prepare an application that is consistent with the expectations of all ASEAN drug regulatory authorities. ASEAN AFTA members include Brunei, Indonesia, Malaysia, Philippines, Singapore, Thailand, Vietnam, Laos, Myanmar, and Cambodia. South Korea introduced a new Clinical Trial Authorization (CTA) process in 2002 for improving its regulatory environment. The procedure allows for applications to be submitted in parallel to institutional review boards/ethics committees and South Korea's regulatory body, Ministry of Food And Drug Safety. This has greatly reduced approval time to between 4 and 8 weeks.

Government of India's Ministry of Health and Family Welfare have notified vide (G.S.R.227 (E) dated 19 March 2019) the Drugs and Clinical Trials Rules, 2019 with an aim to promote clinical research in the country. The new rules will change the regulatory landscape for the approval of new drugs and conduct of clinical trials in the country. The new regulations cover provision for promoting clinical research as well as complex topics such as orphan drug, post-trial access, and pre and post submission meeting. The conditions of waiving local clinical trials under these rules will help provide patients with earlier access to drugs. The approval for clinical trials in 30 working days for indigenous drugs will also speed up the trial process and encourage local drug development. Provision for accelerated product approval under some conditions, especially pre and post submission meetings with authorities may add increased predictability and confidence in the system. The new rules will apply to all new drugs, investigational new drugs for human use, clinical trials, and bioequivalence and bioavailability studies and ethics committees. Overall, the new rules are comprehensive, well-balanced and will likely improve the ethical and quality standards of clinical trials in the country, which also will further benefit patients and industry. Waiving local clinical trial under these rules will help provide earlier access to drugs for patients in India. The deemed approval for clinical trials in 30 working days for indigenous drugs also will speed up the clinical trial process and encourage local drug development. Provision for accelerated product approval under some conditions, along with provision of pre and post submission meeting with the CDSCO office, would add predictability and confidence in the system.¹⁰⁸

MRCTs can facilitate simultaneous global development of a drug and reduce the number of clinical studies conducted separately in each region, thereby minimizing unnecessary duplication of studies.¹⁰⁹ The ultimate goal of MRCT is to bring new medicines to patients globally as fast



as scientifically possible and reduce the drug lag. MRCT also helps in expansion of clinical research into developing countries bringing medical care options to subjects who otherwise may not have access to them. It provides access to more advanced technologies and helps in the development of technical expertise. MRCT provides the sponsors access to otherwise untapped pools of patients, as well as early patient access to new medications.¹¹⁰

¹⁰⁷https://www.cmicgroup.com/files/user/en/solution/pdf/Whitepaper_201710.pdf

¹⁰⁸https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/NewDrugs_CTRules_2019.pdf

¹⁰⁹https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E17/E17EWG_Step4_2017_1116.pdf

¹¹⁰<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4840793/>

XI. Medical Technology Pathways for Innovative Medical Devices

Medical devices are health technologies that include: in vitro diagnostics, any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of: diagnosis, prevention, monitoring, treatment or alleviation of disease, or compensation for an injury, investigation, replacement, modification, or support of the anatomy or of a physiological process, supporting or sustaining life, control of conception, disinfection of medical devices and providing information by means of in-vitro examination of specimens derived from the human body; and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means¹¹¹.

The achievement of health development goals, defined under SDG3, involves the manufacture, regulation, planning, evaluation, acquisition, management, and use of quality, safe and appropriate medical devices which are targeted to specific settings. In accordance with the Health Technologies Resolution WHA60.29 of the World Health Assembly, the mission of the WHO Department of Essential Health Technologies is to enhance access to quality, safe and appropriate medical devices, as well as their use within the reform of primary health care¹¹². Different national governments have taken up policy initiatives to promote innovation in general and in health care in particular. Innovation ecosystem must promote participation of all diverse stakeholders: academic institutions, government, industry and individuals through the creation of new pathways, and programs for medical products and healthcare technologies. India is also engaging in scientific progress and R&D for development of affordable products with supportive technology platforms, network of clinical sites and testing facilities and health technology innovation for meeting critical health needs.

WHO released the second Model List of Essential In Vitro Diagnostics (EDL) in 2019, which extends the first List, published in May 2018. The List recognizes that in vitro diagnostics (IVDs) are essential for advancing universal health coverage, addressing health emergencies and promoting healthier populations, which are the three strategic priorities of the Thirteenth WHO General Programme of Work, 2019–2023¹¹³. The EDL includes 122 test categories comprising 46 general IVD tests, 69 IVDs for specific diseases and 7 test categories for screening of blood donations. Thereafter, India has become the first country to launch its National Essential Diagnostics List (NEDL) in August, 2019¹¹⁴.

National Essential Diagnostics List



Indian Council of Medical Research
Ansari Nagar, New Delhi - 110029, India
2019

¹¹¹https://www.who.int/medical_devices/full_definition/en/

¹¹²https://www.who.int/medical_devices/med_dev_survey/en/

¹¹³https://www.who.int/medical_devices/publications/Standalone_document_v8.pdf?ua=1

¹¹⁴https://www.icmr.nic.in/sites/default/files/Books/NEDL_2019_Final_V2.pdf

¹¹⁵<https://www.fda.gov/about-fda/center-devices-and-radiological-health/cdrh-mission-vision-and-shared-values>

Leading the world in medical device innovation landscape, the United States FDA's Centre for Devices and Radiological Health (CDRH) ensures access of all new technologies and next-generation products to patients with improved safety and effectiveness of medical devices, classified based on their regulatory requirements¹¹⁵.

In 2018, the USFDA approved 106 novel devices, surpassing the 40-year record of 99 set in 2017 and capping eight years of steady improvement¹¹⁶. FDA also published a Strategic Policy Roadmap identifying four priority areas for policy activity in 2018, with one of the priority areas - leveraging innovation and competition to improve healthcare, broaden access, and advance public health goals¹¹⁷. The 510(k) program (Guidance for Industry and Food and Drug Administration Staff) submission of the CDRH for 'Evaluating Substantial



Equivalence in Premarket Notifications', mandates adequate performance data to confirm that the proposed device is as safe and effective as the chosen predicate device¹¹⁸. This is aimed not only at improving the safety and effectiveness of medical devices but also to increase the ability of innovating companies to attract investors, estimate costs, and more quickly bring products to market. In order to address the continuously changing healthcare needs and innovation landscape, the FDA has worked to strengthen the 510(k) Program to meet both patient needs and changes to the device marketplace¹¹⁹.

The Medical Device Innovation Consortium (MDIC) is the first-ever public-private partnership created with the sole objective of advancing medical device regulatory science for patient benefit. Formed in late 2012, MDIC brings together representatives of the USFDA, National Institutes of Health (NIH), USA, Centers for Medicare & Medicaid Services (CMS), Department of Health and Human Services (HHS), industry, non-profits, and patient organizations to improve the processes for development, assessment, and review of new medical technologies. MDIC is the only public-private partnership (PPP) developed to work with government and industry stakeholders in an effort to advance solutions that promote patient access to innovative medical technologies¹²⁰.

In the European Union, medical devices have to undergo a conformity assessment to demonstrate that they meet legal requirements to ensure they are safe and perform as intended¹²¹. EU Member States can designate accredited notified bodies to conduct conformity assessments. The requirement to conduct a clinical evaluation, submit a Clinical Evaluation Report (CER), and receive a CE Mark evidences a strong upfront obligation to ensure quality

¹¹⁶<https://www.fda.gov/news-events/speeches-fda-officials/remarks-alliance-stronger-fda-04102019>

¹¹⁷<https://www.fda.gov/media/110587/download>

¹¹⁸<https://www.fda.gov/media/82395/download>

¹¹⁹<https://www.fda.gov/media/118500/download>

¹²⁰<https://mdic.org/about/mission-purpose/>

¹²¹<https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices>

and anticipate impacts. For in vitro diagnostics (Companion Diagnostics in EU), the in-vitro diagnostic regulation (IVDR) introduces a new classification system and an obligation to undergo a conformity assessment by a notified body. The notified body must seek a scientific opinion from EMA or a national competent authority on the suitability of the companion diagnostic to the medicinal product concerned.

In addition to policy initiatives, capacity building of human workforce and availability of trained manpower are essential to establish an effective innovation system, and is recognised as a need by countries across the globe. Several medtech innovation training platforms have been developed and implemented worldwide using need-driven design approaches to health technology innovation. These include the Stanford India Biodesign Program, Singapore-Stanford Biodesign Program, BioInnovate Ireland, Japan Biodesign, Clinical Innovation Fellowships in Sweden, BioInnovate Ireland and d·HEALTH Barcelona to name a few.

Medical Device sector in India

The Medical Device sector in India is currently valued at \$7-8 billion and is expected to grow to \$20 billion by 2020 and \$50 billion - by 2025 as per industry estimates. The sector is highly import dependent with about 75% of the requirements of the country being met through imports. India has also taken up several policy initiatives towards making India a hub for medical devices through different schemes and programmes. The National Health Policy 2017 recommends strengthening regulation and establishing regulatory body to unleash innovation and entrepreneurial spirit for manufacture of medical devices in India. The Medical Devices Rules 2017 covering requirements of import manufacture, clinical investigations, sale and distribution of medical devices and in-vitro diagnostics has been made effective from January, 2018¹²². Some of the other initiatives are Materiovigilance Program of India (MvPI)¹²³, Medical Technology Assessment Board (MTAB)¹²⁴, strengthened Health Technology Management, enabling landscape created to foster research and innovation under 'Make in India vision to enable access to affordable, safe and effective medical devices globally. The Government also emphasizes on procuring goods including devices from one-stop Government e-Marketplace or GeM portal. The Indian Government policy wants to stimulate innovation and new drug discovery as needed, to meet health needs and to ensure that new drugs discovered and brought into the market are affordable to those who need them most.¹²⁵

The Atal Innovation Mission (AIM) in India is another flagship initiative set up by the NITI Aayog to promote innovation and entrepreneurship across the length and breadth of the country, based on a detailed study and deliberations on innovation and entrepreneurial needs. AIM is also an umbrella innovation organization playing an instrumental role in alignment of innovation policies between central, state and sectoral innovation schemes incentivizing the establishment and promotion of an ecosystem of innovation and entrepreneurship at various levels - higher secondary schools, science, engineering and higher academic institutions, and SME/MSME industry, corporate and NGO levels¹²⁶.

¹²²<https://mohfw.gov.in/sites/default/files/Medical%20Device%20Rules%2C%202017.pdf>

¹²³<http://nhsrcindia.org/archive/terms-reference-research-associates-%E2%80%93-materiovigilance-program-india-mvpi>

¹²⁴<https://dhr.gov.in/mtab>

¹²⁵<https://mohfw.gov.in/sites/default/files/9147562941489753121.pdf>

¹²⁶<https://www.aim.gov.in/overview.php>

The Government of India, through its Department of Biotechnology (DBT), has taken several initiatives - School of International Biodesign (SIB) Programme¹²⁷ and medical device parks dedicated for Medical Device Manufacturing as a one-stop-solution for medical devices to make healthcare products affordable and accessible not only for India but for world at large¹²⁸. To encourage use-inspired discovery research and promote innovation and R&D for development of affordable products for Indian and Global market and support strong technology platforms, create network of clinical sites and testing facilities, certain initiatives of Indian Council of Medical Research (ICMR) with and Ministry of Human Resource Development, such as are IMPRINT (IMPacting Research INnovation and Technology) are also being implemented¹²⁹.

¹²⁷<http://www.biodesignschool.in/>

¹²⁸<http://www.makeinindia.com/article/-/v/sector-survey-medical-devices>

¹²⁹<https://imprint-india.org/about-imprint/imprint-overview>

XII. Medical Products for End Game for HIV/AIDS, Tuberculosis, Malaria

The WHO South East Asia region, home to a third of the world's population, has half the global incident cases of tuberculosis (TB), and a tenth of the estimated burden of malaria and HIV. The risk of disease transmission from travel and migration of people from and within the region highlight the importance of tackling this large disease burden. The increasing resistance to the drugs used to treat malaria, TB, and HIV, and its ability to move across national borders, are challenges to controlling these diseases. Furthermore, drug resistance in malaria, TB, and HIV, and the effect of individual, sociocultural, environmental, and political factors differ between countries, which make containment more difficult¹³⁰. These three diseases present unique challenges in the control of antimicrobial resistance, and require targeted policies.

HIV/AIDS

As the world looks to 2030, and prepares to meet the challenges of an ambitious set of SDGs, WHO developed three global health sector strategies to cover HIV, viral hepatitis, and sexually transmitted infections (STIs). The strategies cover the period 2016-2021 and were endorsed by the Sixty-ninth World Health Assembly on 28 May 2016. The 'Global Health Sector Strategy on HIV 2016–2021: Towards Ending AIDS' builds on the extraordinary public health achievements made in the global HIV response since WHO launched the Special Programme on AIDS in 1986. The strategy promotes a people-centred approach, grounded in principles of human rights and health equity. It will contribute to a radical decline in new HIV infections and HIV-related deaths, while also improving the health and well-being of all people living with HIV. It will guide efforts to accelerate and focus HIV prevention, enable people to know their HIV status, provide antiretroviral therapy and comprehensive long-term care to all people living with HIV, and challenge pervasive HIV-related stigmatization and discrimination¹³¹. It provides the health sector contribution to a broader multisectoral response as outlined in the UNAIDS strategy for 2016–2021. It is also aligned with other relevant global health strategies and plans

The progress report, 2019 on the strategy indicates that reduction in HIV incidence is far behind the targets. HIV mortality has declined but remains too high¹³². Global reporting mechanisms are well established, and major investments have been made in granular, routine data systems. The challenges to achieve success are strengthening data on key populations; and improving the governance of data use for improving programmes. Strong progress has been made towards achieving the 90–90–90 targets and improvements in life expectancy among people living with HIV in countries with a high burden of HIV infection.

In June, 2016, the UN General Assembly made a political commitment to end AIDS by 2030, endorsing the fast-track approach of the UNAIDS. The 'Political Declaration on HIV and AIDS: On the Fast Track to Accelerating the Fight against HIV and to Ending the AIDS Epidemic by 2030' is unflinching in its characterisation of AIDS as "a paramount health, development, human rights and social challenge", and is detailed about the structural, programmatic, and normative

¹³⁰<https://www.bmj.com/content/358/bmj.j3545>

¹³¹<https://apps.who.int/iris/bitstream/handle/10665/246178/WHO-HIV-2016.05-eng.pdf;jsessionid=5B19CA48297BF6C5121E5D42B0793558?sequence=1>

¹³²<https://apps.who.int/iris/bitstream/handle/10665/324797/WHO-CDS-HIV-19.7-eng.pdf?ua=1>

challenges facing the global response to the HIV epidemic¹³³. The 2016 Political Declaration calls on the world to achieve the following goals in support of the 2030 Agenda for Sustainable Development:

1. Reduce new HIV infections to fewer than 500 000 globally by 2020.
2. Reduce AIDS-related deaths to fewer than 500 000 globally by 2020.
3. Eliminate HIV-related stigma and discrimination by 2020.

The Political Declaration affirms that these goals can only be realized with strong leadership and the engagement of people living with HIV, communities and civil society.

WHO recommendations on the use of the HIV/AIDS drugs

In July, 2019, based on new evidence assessing benefits and risks, the WHO recommends the use of the HIV drug dolutegravir (DTG) as the preferred first-line and second-line treatment for all populations, including pregnant women and those of childbearing potential. DTG is a drug that is more effective, easier to take and has fewer side effects than alternative drugs that are currently used. DTG also has a high genetic barrier to developing drug resistance, which is important given the rising trend of resistance to efavirenz (EFV) and nevirapine-based regimens. In 2019, 82 low- and middle-income countries reported to be transitioning to DTG-based HIV treatment regimens. The new updated recommendations aim to help more countries improve their HIV policies¹³⁴.

Tuberculosis (TB)

Through the implementation of the DOTS strategy (1994-2005) and the Stop TB Strategy (2006-2015), countries – especially those with a high burden of TB – established the basics required for providing high-quality TB diagnosis and treatment. It was apparent, however, that while enhancing access to diagnosis and treatment remarkably improved outcomes in terms of reducing suffering and death, it had very little effect on achieving the desired impact in terms of declining the incidence rates and driving down the TB epidemic. This is because TB is not only a biomedical and a public health problem but also a disease associated with poverty.

The reinforced global resolve for intensifying the fight against Tuberculosis (TB) and achieving an end to the global epidemic is illustrated by the adoption of the WHO's End TB Strategy by the World Health Assembly (WHA) in 2014, its endorsement in several WHO Regional Committee meetings during 2015, and the inclusion of “ending the TB epidemic” as a target within the health-related Sustainable Development Goal (SDG) 3 by the United Nations General Assembly in September 2015¹³⁵. The strategy combines a holistic mix of health and social interventions; and aims to end the global TB epidemic, with targets to reduce TB deaths by 95% and to cut new cases by 90% between 2015 and 2035, and to ensure that no family is burdened with catastrophic expenses due to TB. The Global TB Programme, in its 2018 annual report highlights an estimated 1.3 million deaths caused by TB among HIV-negative people in 2017 and an additional 300,000 deaths from TB among HIV-positive people. In countries with a high incidence of TB, WHO guidance issued in 2018 includes a new recommendation to consider testing and treatment for people aged 5 years or more who are household contacts of bacteriologically confirmed pulmonary TB cases. This substantially increases the potential number of people eligible for treatment. In last one year, significant efforts have been made to

¹³³https://www.unaids.org/sites/default/files/media_asset/2016-political-declaration-HIV-AIDS_en.pdf

¹³⁴<https://www.who.int/news-room/detail/22-07-2019-who-recommends-dolutegravir-as-preferred-hiv-treatment-option-in-all-populations>

¹³⁵https://www.who.int/tb/publications/2015/end_tb_essential.pdf?ua=1

address elimination of TB - WHO global ministerial conference on ending TB in the SDG era, leading to the Moscow Declaration to End TB in 2017; and the UN High Level Meeting on TB in September 2018.

The main health-care interventions to prevent new infections of *Mycobacterium tuberculosis* and their progression to TB disease are treatment of latent TB infection and vaccination of children with the Bacille Calmette-Guérin (BCG) vaccine. TB preventive treatment for a latent TB infection is expanding, but most of those for whom it is strongly recommended are not yet accessing care, whereas coverage of BCG vaccination is high. In 2017, 158 countries reported providing BCG vaccination, of which 120 reported coverage of at least 90%. Urgent action is required to improve the coverage and quality of diagnosis, treatment and care for people with drug-resistant TB¹³⁶. Funding for the provision of TB prevention, diagnostic and treatment services has more than doubled since 2006 with domestic funding having more than tripled between 2016 and 2018. The End TB Strategy milestones can only be achieved if TB diagnosis, treatment and prevention services are provided within the context of progress towards universal health coverage (UHC), and if there is multi-sectoral action to address the social and economic factors that drive TB epidemics.

The new treatment guidelines of the WHO for multidrug-resistant TB (2018) prioritize oral drugs, such as bedaquiline (diarylquinoline antimycobacterial agent), and minimize injectables, which can cause patients pain and distress and serious adverse events that lead to interruption of treatment¹³⁷. Fluoroquinolones (levofloxacin or moxifloxacin), bedaquiline and linezolid are strongly recommended for use in longer regimens, which are completed with other medicines ranked by their relative balance of effectiveness to potential toxicity. In 2019, 'WHO consolidated guidelines on drug-resistant tuberculosis treatment' have been released. The policy recommendations in these guidelines have been developed by WHO-convened Guideline Development Groups (GDGs), using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to summarize the evidence, and formulate policy recommendations and accompanying remarks¹³⁸.

WHO has released a multisectoral accountability framework to accelerate progress to end the TB epidemic. The framework was requested by the World Health Assembly and the UN General Assembly in 2018. WHO seeks to enable its adaptation and use by Member States and their partners at country, regional and global levels in 2019. At the UN General Assembly high-level meeting on the fight against TB in September 2018, Dr Tedros Adhanom Ghebreyesus, the Director-General of WHO, stated, "We must hold each other accountable for the promises we are making today. That's why we are developing a multisectoral accountability framework with four components: commitment, action, monitoring and review, to ensure we match our talk with real, lasting change." The framework (MAF-TB) aims to support the process of defining who is accountable, what they are accountable for, and how they will be held accountable, at country and local levels, as well as at regional and global levels. There are four components of the MAF-TB that form a cycle for strengthening accountability: Commitments, Actions, Monitoring and Reporting, and Review. The MAF-TB provides guidance on defining elements under each of these components, at national level as well as at global and regional levels. Some highlighted accountability measures are not yet established in many countries, and others need urgent strengthening¹³⁹.

¹³⁶https://www.who.int/tb/publications/global_report/tb18_ExecSum_web_4Oct18.pdf?ua=1

¹³⁷https://www.who.int/tb/features_archive/updated-treatment-guidelines-multidrug-rifampicin-resistant-TB/en/

¹³⁸<https://www.who.int/tb/publications/2019/consolidated-guidelines-drug-resistant-TB-treatment/en/>

¹³⁹https://www.who.int/tb/features_archive/multisectoral-accountability-framework-to-end-TB/en/

Malaria

Malaria is a disease of the most vulnerable: the very young and the poor. Every year, there are about 219 million cases of the disease, and more than 400,000 deaths. Children under 5 years of age account for 61% of all malaria deaths while over 90% of malaria deaths occur in sub-Saharan Africa¹⁴⁰. Eradicating malaria would have the greatest beneficial impact on the world's most vulnerable populations. Over the last 15 years, the world has seen unprecedented progress in the fight against malaria. Globally, the rate of new malaria cases has declined by 37%. Malaria death rates have plunged by 60%. In the last decade alone, 7 countries have been certified by WHO as malaria-free. In 2015, the WHO European Region, comprised of 53 countries, reported zero indigenous cases of the disease. UN Member States are increasingly calling for malaria elimination in their own country or region, prompting renewed discussion around the ultimate goal of global malaria eradication¹⁴¹.

In 2015, the Sixty-eighth World Health Assembly unanimously endorsed a bold plan - the Global technical strategy for malaria 2016– 2030 - to rid the world of 90% of the burden of death and disease due to malaria by 2030 and to eliminate this infection from at least 35 more countries. These ambitious yet achievable targets are considered essential stepping stones on the path to achieving a world free of malaria, the vision that was reaffirmed in the plan¹⁴². According to a WHO analysis published in 2016, 21 countries (out of 35) have the potential to eliminate malaria by 2020. These 21 malaria-eliminating countries are part of a concerted effort known as the E-2020 initiative¹⁴³.

Several other initiatives of the WHO include Malaria Vaccine Implementation Programme (MVIP) wherein Ghana, Malawi and Kenya are participating in pilot programme for RTS,S/AS01 (RTS,S) - world's first malaria vaccine¹⁴⁴. Medicines for Malaria Venture (MMV), a global product development partnership (PDP) in antimalarial drug research has a mission to reduce the burden of malaria in disease-endemic countries by discovering, developing and delivering new, effective and affordable antimalarial drugs¹⁴⁵.

The RBM Partnership to End Malaria is the largest global platform for coordinated action towards a world free from malaria; comprised of over 500 partners - from community health worker groups and researchers developing new tools, to malaria-affected and donor countries, businesses and international organisations¹⁴⁶. In response to the worsening malaria situation, WHO and the RBM Partnership to End Malaria have catalysed the country-led High Burden High Impact (HBHI) approach¹⁴⁷, providing a renewed focus on making a durable impact in countries with the highest burden of malaria and getting back on track to achieve the 2030 targets in the Global technical strategy for malaria 2016-2030. The approach will initially focus on getting the 11 highest burden countries back on track, 10 of which are in Africa. By taking the HBHI approach, countries will establish an enabling environment for increasing and maximizing the use of resources for malaria impact. Four mutually reinforcing response elements feed into tangible actions and concrete outcomes:

- Political will translated into better use of resources and action;
- Information used more strategically;
- Technical guidance improved;
- Response efforts better coordinated.

¹⁴⁰<https://apps.who.int/iris/bitstream/handle/10665/275867/9789241565653-eng.pdf>

¹⁴¹<https://www.who.int/malaria/news/2016/advisory-group-malaria-eradication/en/>

¹⁴²<https://www.who.int/publications-detail/strategic-advisory-group-malaria-eradication-executive-summary>

¹⁴³<https://www.who.int/malaria/media/e-2020-initiative-qa/en/>

¹⁴⁴<https://www.who.int/malaria/media/malaria-vaccine-implementation-qa/en/>

¹⁴⁵<https://www.mmv.org/about-us/what-we-do/overview-our-work>

¹⁴⁶<https://endmalaria.org/about-us>

¹⁴⁷High burden to high impact: a targeted malaria response. Geneva: World Health Organization (WHO/CDS/GMP/2018.25; <http://apps.who.int/iris/bitstream/handle/10665/275868/WHO-CDS-GMP-2018.25-eng.pdf>)

The approach will be rolled out to all malarious countries in Africa as we progress towards a malaria-free continent.

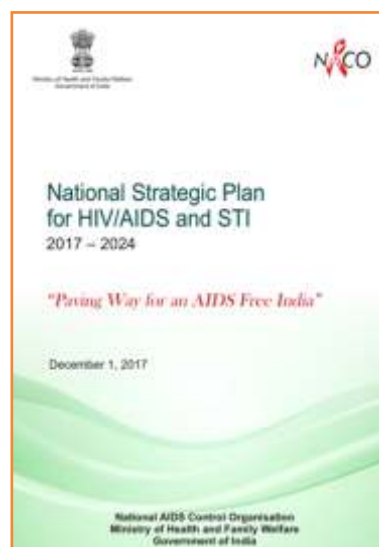
A 3 year study undertaken by the WHO Strategic Advisory Group on Malaria Eradication (SAGme) reports and calls for more investment in research and development of new tools and approaches to fight malaria, stronger universal health coverage so that everyone can access the services they need, and better surveillance to guide a more targeted malaria response¹⁴⁸.

Policy Initiatives by India

Based on India HIV Estimation 2017 report, National adult (15–49 years) HIV prevalence in India is estimated at 0.22% (0.16% – 0.30%) in 2017. In 2017, adult HIV prevalence is estimated at 0.25%(0.18-0.34) among males and at 0.19% (0.14-0.25) among Females.vThe adult HIV prevalence at national level has continued its steady decline from an estimated peak of 0.38% in 2001-03 through 0.34% in 2007, 0.28% in 2012 and 0.26% in 2015 to 0.22% in 2017¹⁴⁹. The National AIDS Control Programme (NACP), launched in 1992, is being implemented as a comprehensive programme for prevention and control of HIV/AIDS, in addition to the National AIDS Control & Prevention Policy adopted in 2002. Apart from this, policies have extensive guidelines on the management of common opportunistic infections, malignancies among adult/adolescent PLHA and operational guidelines for ART centres to standardise ART services across the country. The National Policy on Blood Banks ensures adequate supply of safe blood and blood components.

The Government of India's National AIDS Control Organization (NACO), in its approach to reach 'the last mile' has implemented a seven-year National Strategic Plan on HIV/AIDS and Sexually Transmitted Infections (STI), 2017-24¹⁵⁰. By 2020, the focus of the national programme will be on achieving the following fast track targets¹⁵¹:

- (i) 75% reduction in new HIV infections,
- (ii) 90-90-90: 90% of those who are HIV positive in the country know their status, 90% of those who know their status are on treatment and 90% of those who are on treatment experience effective viral load suppression,
- (iii) Elimination of mother-to-child transmission of HIV and Syphilis, and
- (iv) Elimination of stigma and discrimination Paving Way for an AIDS Free India



By 2024, the further achievements envisaged are:

- (i) 80% reduction in new HIV infections,
- (ii) Ensuring that 95% of those who are HIV positive in the country know their status, 95% of those who know their status are on treatment and 95% of those who are on treatment experience effective viral load suppression

¹⁴⁸<https://www.who.int/publications-detail/strategic-advisory-group-malaria-eradication-executive-summary>

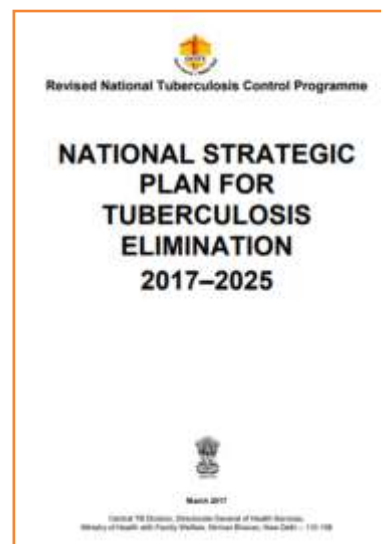
¹⁴⁹<http://naco.gov.in/hiv-facts-figures>

¹⁵⁰<http://naco.gov.in/national-strategic-plan-hivaids-and-sti-2017-24>

¹⁵¹<http://naco.gov.in/sites/default/files/Paving%20the%20Way%20for%20an%20AIDS%2015122017.pdf>

To this effect, two key achievements in early 2017 to 'Ending of AIDS by 2030' include the enactment of the 'HIV/AIDS Bill' as a law protecting the rights of people living with and affected by HIV as well as the announcement and implementation of the 'Test and Treat' policy in line with global guidelines.

The National TB Programme (NTP) was launched by the Government of India in 1962 in the form of District TB Centre model involved with BCG vaccination and TB treatment. In 1978, BCG vaccination was shifted under the Expanded Programme on Immunisation. The Government of India revitalized NTP as Revised National TB Control Programme (RNTCP) in 1993. DOTS was officially launched as the RNTCP strategy in 1997 and by the end of 2005, the entire country was covered under the programme. National Strategic Plan for Tuberculosis Control 2012-2017 was documented with the goal of 'universal access to quality TB diagnosis and treatment for all TB patients in the community'. Significant interventions and initiatives were taken during NSP 2012-2017 in terms of mandatory notification of all TB cases, integration of the programme with the general health services (National Health Mission), expansion of diagnostics services, programmatic management of drug resistant TB (PMDT) service expansion, single window service for TB-HIV cases, national drug resistance surveillance and revision of partnership guidelines¹⁵².



India has a Revised National Tuberculosis Control Programme (RNTCP) to prevent and control TB in the country with integrated four pillars of “detect – Treat – Prevent – Build” (DTPB) and aims to eliminate TB by 2025¹⁵³. In the High Level Meeting on Tuberculosis at 73rd session of United Nations General Assembly (UNGA), Union Health Minister Shri JP Nadda stated that Prime Minister Shri Narendra Modi has shown personal commitment to tackle TB head-on as India plans to eliminate TB by 2025, five years ahead of the SDG target of 2030, by launching the TB Free India Campaign. In his address, Shri Nadda said that India's National Health Policy 2017 clearly articulates the vision of a TB free India. He added that India has allocated US\$ 430 million for implementation of the Plan in the current year, which is an increase of 54% over last year. India has also established its own TB research consortium to accelerate research efforts in TB, in addition to the launch of the BRICS TB Research Network.

Malaria Elimination in India

India contributes 70% of malaria cases and 69% of malaria deaths in the South-East Asia Region. However, a WHO projection showed an impact in terms of a decrease of 50–75% in the number of malaria cases by 2015 in India (relative to 2000 baseline), which showed that the country has been on track to decrease case incidence 2000–2015. In November 2014, the Asia Pacific Leaders Malaria Alliance (APLMA) representing 18 countries, including India, agreed to the goal of a region free of malaria by 2030¹⁵⁴. The NFME has clearly defined goals, objectives, strategies, targets and timelines and will serve as a roadmap for advocating and planning malaria elimination throughout the country in a phased manner. The objectives are to: (1)

¹⁵²https://www.nhp.gov.in/revised-national-tuberculosis-control-programme_pg

¹⁵³https://www.nhp.gov.in/revised-national-tuberculosis-control-programme_pg

¹⁵⁴<https://pib.gov.in/newsite/PrintRelease.aspx?relid=183767>

¹⁵⁵https://apps.who.int/bitstream/handle/10665/246096/national_framework_malaria_elimination_india_2016_2030.pdf?sequence=1&isAllowed=y

Eliminate malaria from all Category 1 and Category 2 states/UTs (26) with low and moderate-transmission of malaria by 2022; (2) Reduce the incidence of malaria to less than one case per 1000 population per year in all states/UTs and their districts and achieve malaria elimination in 31 states/UTs by 2024; (3) Interrupt indigenous transmission of malaria in all states/UTs (Category 3) by 2027; and (4) Prevent re-establishment of local transmission of malaria in areas where it has been eliminated and maintain malaria-free status nationally by 2030.

In 2019, ICMR launched Malaria Elimination Research Alliance (MERA) – India, which is a conglomeration of partners working on malaria control. The principal activity of the alliance is to prioritise, plan, conduct, scale up and translate relevant research in a coordinated and combinatorial way in order to have a tangible impact of this research on the population at risk for malaria. MERA India aims to harness and reinforce research in coordinated and combinatorial ways in order to achieve tangible impact on malaria elimination¹⁵⁶.

India also shares a sustained partnership with the Global Fund since 2002 both as recipient and as a donor. Global Fund support with investment of US \$ 2.0 billion so far has made significant contribution in attaining targets related to HIV/AIDS, TB and Malaria reduction. In the current funding cycle (2018-21), the Global Fund has allocated US\$ 500 million to India. India has announced a contribution of US\$ 22 million to the Global Fund for AIDS, TB and Malaria (GFTAM) for the 6th replenishment cycle (2020-22), an increase of 10% over the amount contributed in the 5th cycle¹⁵⁷.

The WHO Global Health Observatory is a gateway to health-related statistics for more than 1000 indicators for its 194 Member States. Data are organized to monitor progress towards the SDGs, including health status indicators to monitor progress towards for the overall health goal, indicators to track equity in health indicators, and the indicators for the specific health and health-related targets of the SDGs¹⁵⁸.

¹⁵⁶<https://icmr.nic.in/content/launch-malaria-elimination-research-alliance-mera-india-and-stakeholders-meet-icmr>

¹⁵⁷<https://pib.gov.in/newsite/PrintRelease.aspx?relid=192975>

¹⁵⁸<https://www.who.int/gho/en/>

XIII. Global Partnerships for Drug Discovery, Innovation and Technology Development: Scaling up Adaptive Technology Solutions for Medical Products

Achieving the goal of healthy lives and well-being for all can be accelerated through investments in research and innovation, made accessible on an equitable basis. Today, there is a vibrant community of researchers and innovators across the academic and private sector working to develop solutions for health problems, from basic, fundamental science, to new medical products and devices, to system-level and social sciences research.

Various World Health Assembly Resolutions, have been focusing on the need of promoting innovation to achieve the SDGs such as WHA69.11 (2016): Health in the 2030 Agenda for Sustainable Development, WHA69.20 (2016): Promoting innovation and access to quality, safe, efficacious and affordable medicines for children and WHA68.18 (2015): Global strategy and plan of action on public health, innovation and intellectual property.

A strong evidence base will need to be developed, such as analyses of product pipelines and funders' portfolios to identify gaps and areas of action which will help in identifying much larger areas for collaboration and future mobilisation of the global health research community post-UNGA2019.

In line with the Global strategy and plan of action on public health, innovation and intellectual property, which recommends prioritizing needs for and promoting research and development, WHO is playing a role in facilitating research and development for neglected areas, where there is a compelling unmet public health need for new products, including by coordinating the efforts of different actors, setting research and development priorities, identifying associated gaps, defining desired product profiles and facilitating the development of affordable, suitable health products. The Global Observatory on Health Research and Development is central to setting priorities for product development and contributing to coordinated actions on health research and development. The R&D Blueprint supports the development of a global preparedness plan for addressing future epidemics. WHO, together with the Drugs for Neglected Diseases initiative, has set up the Global Antibiotic Research & Development Partnership (GARDP) to develop new treatments for bacterial infections.

Many potential solutions that could have significant positive impact on realizing SDG 3 have been successfully tested in the pilot phase. Yet there are often barriers and delays to the adoption of these solutions, sustainably and at scale, in the countries that need them most. The research accelerator will, through a time-bound process, establish a sustainable roadmap for global health research, development, innovation and access to 2030 and beyond.

In addition to the overarching aim of realigning (international and domestic) research investments with country needs to achieve universal health coverage (UHC), healthier populations and protection from health emergencies, the roadmap will include the following four elements¹⁵⁹:

¹⁵⁹Accelerator paper 5

- Sustaining investment in new ideas: the accelerator will identify best practices for research and pipeline coordination, innovation hubs and other routes for generating new knowledge and propositions for health-improving innovation.
- Ensuring that promising innovations reach those who need them: organizations will work together to identify promising innovations ready to transition to scale, and participate in partnerships with governments, funders and the private sector to help innovations translate to impact.
- Optimising the path to scale-up: the accelerator will look at existing routes to scale (including the role of tools such as technical guidance and innovation marketplaces) and recommend improvements to ensure that barriers are quickly removed.
- Enabling sustainable scale-up at the country level: the accelerator will explore how to shift priorities for research and innovation to the country level (particularly in LMICs), with assistance provided to countries to establish local priorities and modalities for bringing innovations to scale and ensuring equitable access.

There is a need to address three areas: Optimising the global research system for identifying international systems-level improvements which require coordination and alignment across the sector, Scaling up innovation for identifying catalytic actions for national and international organisations to work together to achieve scale up and impact and elevating country priorities for consulting directly with countries to create better alignment between national needs and internationally-commissioned research and innovations.

WHO Health Innovation Group (WHIG) is a voluntary group of interested WHO colleagues who jointly promote and pursue health innovation within the Organization. The group also strives to promote WHO's image and position on health innovation to the outside world¹⁶⁰. WHIG is open to all WHO staff and it offers an open forum on health innovation, limited to only product development. Keeping in view WHO's vision, mandate and its leadership priorities, the group has adopted a comprehensive working definition of health innovation as follows:

- Health innovation is to identify new or improved health policies, systems, products and technologies, and services and delivery methods that improve people's health and well-being.
- Health innovation responds to unmet public health needs by employing new ways of thinking and working with a special focus on the needs of vulnerable populations;
- Health innovation aims to add value in the form of improved efficiency, effectiveness, quality, sustainability, safety and/or affordability;
- Health innovation can be preventive, promotive, palliative, curative, rehabilitative and/or assistive care;
- WHO engages in health innovation to achieve universal health coverage within the context of the Sustainable Development Goals.

Technology can play an important role to harness the innovative energy, addressing the challenges and realizing the opportunities. Partnerships involving collaborations between the pharmaceutical industry, government agencies, academics, foundations, and independent non-profit organizations hold promise for addressing unmet needs in medical product research and development. Effective partnerships can enhance access to innovation, reduce risk, and manage costs and may provide a means for steering research and development investment to address societal objectives. The numerous public-private partnerships (PPPs) that have

¹⁶⁰<https://www.who.int/life-course/about/who-health-innovation-group/en/>

emerged over the past 20 years reflect different models of operation and different approaches to aspects such as the partnership objective, participants and their roles, intellectual property (IP) policies, funding sources, and governance.

The leaders confirmed their support at the G20 Hangzhou Summit in 2016 to “dialogue and cooperation on innovation, which covers a wide range of domains with science and technology innovation at its core” to “achieve innovation-driven growth and the creation of innovative ecosystems”, and endorsed the G20 Blueprint on Innovative Growth and the G20 Innovation Action Plan, based on the discussion at three Task Forces on Innovation, New Industrial Revolution and Digital Economy as well as the Science, Technology and Innovation (STI) Ministers’ Meeting where. STI can be an important consideration for making the best use of limited resources in the pursuit of achieving the 2030 Agenda. Under the Japanese Presidency, the G20 shared the view that STI could play an important role to support the implementation of the 2030 Agenda by launching the “Guiding Principles for the Development of STI for SDGs Roadmaps”.¹⁶¹

Technological innovation in medicine covers the wide range of events by which a new medical technology is discovered or invented, developed, and disseminated into health care. One of the most vulnerable links in the innovation chain is the development phase, the “D” of R&D, in which research findings are brought into clinical practice. More specifically, medical technology development can be defined as a multi-stage process through which a new biological or chemical agent, prototype medical device, or clinical procedure is technically modified and clinically evaluated until it is considered ready for general use¹⁶².

There is a need to accelerate, re-start, and recover the development of new and abandoned drug candidates that address public health priorities and vulnerable populations (e.g. people living with sexually-transmitted infections (STIs), newborns) and exploring novel and innovative drug development approaches with a longer-term view towards meeting patients’ needs.

For drug discovery, FDA is conducting a **Model-Informed Drug Development (MIDD)** Pilot Program to facilitate the development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources, referred to as MIDD approaches¹⁶³. MIDD approaches use a variety of quantitative methods to help balance the risks and benefits of drug products in development. When successfully applied, MIDD approaches can improve clinical trial efficiency, increase the probability of regulatory success, and optimize drug dosing/therapeutic individualization in the absence of dedicated trials¹⁶⁴.

Artificial Intelligence in Drug Discovery and Development: Emerging Technologies and Applications¹⁶⁵ - Quantum computing tools have the potential to address many early-phase biopharmaceutical challenges such as reaction rate prediction, combinatorial optimization, and accurate simulation of atoms and molecules. Metabolomics another emerging field that analyzes metabolites to determine their biological function can be enhanced with AI-based data processing and analysis to better understand disease pathway activity and identify appropriate

¹⁶¹https://g20.org/pdf/documents/en/annex_11.pdf

¹⁶²<https://www.ncbi.nlm.nih.gov/books/NBK235486/>

¹⁶³<https://www.fda.gov/drugs/development-resources/model-informed-drug-development-pilot-program>

¹⁶⁴<https://www.fda.gov/drugs/development-resources/model-informed-drug-development-pilot-program>

<https://www.diaglobal.org/en/resources/insider->

¹⁶⁵<https://globalforum.diaglobal.org/issue/august-2019/ai-in-drug-discovery-and-development-emerging-technologies-and-applications/>

interventions. In addition to helping identify digital biomarkers to power new and less fragile endpoints, AI-based approaches could influence a number of clinical research functions from protocol design and patient identification to endpoint selection and process automation.

During the last decades, the majority of the 20 largest research-based pharmaceutical companies have increased efforts to provide access to essential medicines in developing countries, e.g., by supporting or participating in product development partnerships (PDPs)¹⁶⁶. The PDP model ensures a holistic pipeline approach rather than being limited to a single portfolio. These efforts de-link the cost of final products from R&D expenditures by recruiting diverse funding sources rather than relying on retroactive cost recuperation via the exercise of IP rights¹⁶⁷.

The Medical Technology landscape is changing, with challenges in the form of dynamic regulatory requirements, market forces driving the need to introduce new medical device and diagnostic products, and innovative combination products, under difficult pricing and profitability conditions. There is a continuous need for specialist guidance and solutions throughout the entire product lifecycle, from concept-to-market.

The Consultative Expert Working Group on Research and Development (CEWG) was established by the World Health Assembly in 2010 with the principal task of deepening the analysis and work done by the previous Expert Working Group on Research and Development. The Consultative Expert Working Group (CEWG) on Research and Development had also highlighted open approaches to R&D and innovation, pooled funds, direct grants to companies, milestone prizes, end prizes and patent pools and the general principle of de-linking the costs of R&D from the price of the medicine, meaning that the investor does not have to recoup its R&D investment through the sales revenues. The report was also discussed by the WHO Member States in an open ended meeting in November 2012 and there was an agreement on a strategic work plan that included the creation of a WHO global health R&D observatory, implementation of a number of health R&D demonstration projects, and exploration of a potential financing mechanism for pooled contributions and coordination.

Public-private partnerships, and PDPs, are vehicles suitable for delivering healthcare and strengthening healthcare systems. Such multi-stakeholder efforts are able to ensure product registration, increase local production and distribution capacity, and ensure governance for global health, e.g., adoption of new health technologies in national treatment policies in disease-endemic countries. PDPs strengthen research capacity in LMICs by building infrastructures at trial sites, providing equipment and setting up training in good clinical practice (GCP) and dedicated disease-specific research platforms in endemic countries. To achieve its objectives, PDPs partner with different stakeholders, such as high-income country programs and platforms, national governments and philanthropic organizations¹⁶⁸. outcomes as well as increase the employment of labor between public and private sectors. Product development partnerships (PDPs) with not-for-profit entities and industry players, major philanthropic funding, etc. may significantly increasing the number of products in development, and identifying pathways regarding existing research gaps.

- They integrate public-sector and private-sector approaches, and generally use industry practices in their R&D activities.

¹⁶⁶<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5725781/#B19>

¹⁶⁷<https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/11869/Tuttle%20Thesis%204-25.pdf>

¹⁶⁸<https://www.ncbi.nlm.nih.gov/pubmed/24028246/>

- They manage neglected diseases R&D portfolios and they target one or more neglected disease.
- They are created in order to pursue public health objectives rather than commercial gains, and also in order to provide funding to cover existing research gaps.
- They ensure that the developed products are affordable.

The public–private partnerships in drug discovery -The public and private sector should be engaged in providing infrastructure and expertise to conduct high-throughput screening (HTS) and identification of leads for pharmaceutical development, as well as training of fellows from developing countries. It should be capable to supply of compound libraries, expertise with pharmaceutical research, development, and commercialization activities. World Health Organization and other such organisations shall contribute oversees the management and technical review of the collaboration, supplies molecular targets through academic collaborators to support HTS, provides access to screening, medicinal chemistry, and DMPK networks, and sponsors fellows from Africa to be trained at NCDS as part of the collaboration.

Biomedical Advanced Research and Development Authority (BARDA), USA is responsible for developing and procuring technologies and countermeasures to protect the nation against natural and man-made threats. BARDA has delivered solutions to protect our country and the world from threats like Anthrax, Smallpox, Ebola, Pandemic Influenza, and many others. Since it was established in 2006, as part of the Pandemic and All Hazards Preparedness Act, BARDA has facilitated 42 FDA approvals, licensures, and clearances for products addressing a wide range of chemical, biological, radiological, and nuclear threats; pandemic influenza; and emerging infectious diseases. BARDA's mission is accomplished through successful public-private partnerships with industry to share risk, improve efficiency, and accelerate development all while sustaining a marketplace that guarantees continued access to the vaccines, therapeutics, diagnostics, and other medical products that are vital to our national health security.

DRIVE (Division of Research, Innovation, and Ventures) was established by the Biomedical Advanced Research and Development Authority (BARDA), part of the Assistant Secretary for Preparedness and Response (ASPR), within the United States Department of Health and Human Services (HHS)¹⁶⁹. DRIVE is forming novel Public-Private Partnerships, and an ecosystem of restless innovation. Approaches could include non-dilutive funding through DRIVE-X or dilutive funding through DRIVE Launch or DRIVE Ventures. DRIVE is building an ecosystem of restless innovators that includes investors, companies, and research teams offering solutions to a broad range of national health security threats. These include drugs and indicators to reduce illness and death from sepsis, technologies and processes to identify biological and other threats, and tools and techniques to mitigate the damages and loss of life associated with catastrophic events. Accelerate the development and availability of transformative technologies and approaches to protect Americans from health security threats. Seek new ideas and new approaches to find solutions that will prevent and protect against health security threats.

The **African Network for Drugs and Diagnostics Innovation (ANDI)**, has also been created to develop sustainable platform for R&D innovation in Africa to address Africa's own health needs¹⁷⁰. Its mission is to promote and sustain African-led health product innovation that addresses African public health needs through the assembly of research networks, and build

¹⁶⁹<https://drive.hhs.gov/>

¹⁷⁰<https://www.who.int/tdr/partnerships/initiatives/andi/en/>

capacity to support human and economic development. The current progress of the network includes 3 successful stakeholders meetings in collaboration with the Kenyan government, Development and endorsement of the strategic business plan for ANDI by stakeholders, review of the first Pan-African Centers of Excellence in health innovation completed, establishment of 5 regional hubs in the 5 regions of Africa, establishment and funding of ANDI portfolio of projects.

In the late 1990s an innovative collaboration model for R&D for neglected diseases emerged in the form of public-private partnerships (PPPs) that came to be known as product development partnerships (PDPs). PDPs were created with a desire to generate innovative approaches to alleviate the global burden of neglected diseases by taking the expertise and knowledge of both the private and public sectors, and exploiting each of their strengths to find the most efficient and effective solutions. PDPs address the lack of commercial incentive to undertake R&D for vaccines, diagnostics, and drugs for neglected diseases of the developing world¹⁷¹.

The GARD-P addresses global public health and the specific needs of low- and middle-income countries and targets products that industry will not develop due to foreseen lack of incentives, pilots the use of alternative incentive models that support conservation of and access to new antibiotics based on DNDi's experience in implementing alternative R&D models for neglected diseases, ensures that new antibiotics are affordable to all in need worldwide.

The Drugs for Neglected Diseases initiative (DNDi), is a non-profit drug research and development (R&D) organization and Product Development Partnership (PDP) which was established in 2003 by 7 founding organizations such as Médecins Sans Frontières (MSF), the Pasteur Institute, The Specific Programme for Research and Training in Tropical Diseases (WHO-TDR), etc. DNDi has worked mainly on the development of new treatments for neglected tropical diseases (NTDs), which is difficult to achieve under market economy conditions. DNDi has promoted overall drug discovery research including the screening of drug candidates, hit to lead, lead optimization, pre-clinical and clinical studies in the area of infectious diseases with a focus on malaria, sleeping sickness (human African trypanosomiasis; HAT), Chagas disease, leishmaniasis, filarial diseases and pediatric formulations for HIV treatment..

DNDi has established regional disease-specific platforms, which bring together partners in disease-endemic countries to strengthen existing clinical research capacity, as well as to build new capacity where necessary. In Africa, two platforms have been set up: the Leishmaniasis East Africa Platform (LEAP) and the HAT platform, and in Latin America, DNDi has created the Chagas Platform. Since its inception in 2003, DNDi has delivered six treatments: two fixed-dose anti-malarials (ASAQ and ASMQ), nifurtimox-eflornithine combination therapy (NECT) for late-stage sleeping sickness, sodium stibogluconate and paromomycin (SSG&PM) combination therapy for visceral leishmaniasis in Africa, a set of combination therapies for visceral leishmaniasis in Asia, and a pediatric dosage form of benznidazole for Chagas disease¹⁷². DNDi's R&D Portfolio is covered over 45 projects and more than 20 new chemical entities, with over 20 ongoing clinical trials.

Malaria Medicines Venture (MMV) is another leading PDP in the field of antimalarial drug research and development. Its mission is to reduce the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, effective and affordable antimalarial drugs. Since its foundation in 1999, MMV has developed and brought to registration

¹⁷¹<https://www.mmv.org/partnering/pdp-model>

¹⁷²www.dndi.org

four new medicines with its partners: Pyramax®, co-developed with Shin Poong; Eurartesim® with Sigma-Tau; Guilin's artesunate injection for the treatment of severe malaria, Artesun®; and Coartem® Dispersible, a child-friendly formulation developed with Novartis. Since 2009, over 200 million courses of Coartem Dispersible treatment have been supplied to 50 malaria-endemic countries; and since prequalification in 2010, an estimated 12 million vials of artesunate injection have been delivered, saving 80,000 - 90,000 additional lives.

Managing the largest portfolio of antimalarial R&D projects ever assembled, of over 65 projects, MMV has seven new drugs in clinical development addressing unmet medical needs in malaria, including medicines for children, pregnant women and relapsing malaria, and drugs that could support the elimination/eradication agenda. MMV's success in research and access & product management comes from its extensive partnership network of over 300 pharmaceutical, academic and endemic-country partners in 50 countries. MMV's vision is a world in which innovative medicines will cure and protect the vulnerable and under-served populations at risk of malaria, and ultimately help to eradicate this terrible disease¹⁷³. MMV has defined five Target Candidate Profiles, corresponding to different clinical attributes needed for the TPPs, and built a strong portfolio of molecules with diverse or competing mechanisms to combat resistance.

Initiatives promoting 'out of the box' solutions

Other Product development partnerships (PDPs) focusing on drugs are Institute of One World Health (<http://www.iowh.org/>) and Global Alliance for TB Drug development¹⁷⁴ (<http://tballiance.org/>).

The **mobile health application (mHealth) Text4Baby**, providing free health information to expectant mothers by means of text messages, is a PPP that, through a network of hundreds of partners, scales up its services. PPPs can improve both health products and services delivery by scaling their programs to a national level, involving health workers and communities¹⁷⁵. These efforts de-link the cost of final products from R&D expenditures by recruiting diverse funding sources rather than relying on retroactive cost recuperation via the exercise of IP rights¹⁷⁶.

PDPs directed toward neglected tropical diseases (NTDs) were the first collaborative efforts to tackle inequities in the health sector. In 1987, Merck & Co. donated ivermectin (Mectizan®) to treat onchocerciasis or river blindness, first distributed by the African Programme for Onchocerciasis Control (APOC), a partnership between the World Bank, the WHO, and non-governmental organizations (NGOs) in West-Africa, and expanded later to Africa and America¹⁷⁷.

In 2001, Nelson Mandela's government asked Indian generic manufacturer, Cipla, to make ARV drugs for the South African public at prices they could afford. The backlash from pharmaceutical companies and developed countries was immense, but with the support of civil society groups that successfully argued against the logic of big pharma, the South African government successfully utilized a TRIPS-compliant compulsory license and parallel importation provisions to lower the price of ARVs to about US\$113 per person per year. With generic drugs available at this cost, the country has been able to increase coverage and lower expenditure at the same time, thus slowing a mounting epidemic¹⁷⁸.

¹⁷³www.mmv.org

¹⁷⁴(<http://www.iowh.org/>) and (<http://tballiance.org/>).

¹⁷⁵<https://www.ncbi.nlm.nih.gov/pubmed/23353680/>

¹⁷⁶<https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/11869/Tuttle%20Thesis%204-25.pdf>

¹⁷⁷<https://www.liebertpub.com/doi/10.1089/blr.2013.9929>

¹⁷⁸<https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/11869/Tuttle%20Thesis%204-25.pdf>

Technological interventions like tele-consultation, and mHealth involving the use of telecommunication and multimedia technologies integrated with mobile and wireless healthcare delivery system have been emerging in recent times. Using mobile technology offers a tremendous opportunity for developing countries as India to advance in health care delivery by effectively utilising scarce resources. The vastly underserved healthcare market combined with high mobile phone penetration and rapidly growing smart phone adoption creates enabling environment condition for mHealth adoption in India. mHealth, being user friendly and cost effective, would be an interesting initiative in developing world¹⁷⁹.

The power of public–private collaborations is the closer integration of subject matter experts with the drug development expertise and the resources to translate these novel findings to drugs. The shared goal of improving human health and realizing the potential of the research motivates these collaborations, but reaching a success milestone requires building of trust, open-minded debate, and incentives appropriate to each environment¹⁸⁰.

Moreover, knowledge and technology transfer should happen in both directions. The technology applied in low-resource programs can stimulate innovation in developed countries, for example, by using text messages and interactive voice recognition systems instead of smartphone applications or by targeting the markets of the underserved such as elderly or immigrant communities this way, an innovation continuum can exist¹⁸¹.

Biocon India, has developed insulins in India indigenously through a proprietary technology in the early 2000s, and developed and delivered two affordable novel biologics for the benefit of cancer and psoriasis patients in India. India is therefore proving its mettle as a “laboratory for the world” that can deliver affordable innovation and a growing number of collaborative efforts are succeeding in delivering products and services going a long way in ensuring that the right to healthcare becomes truly universal¹⁸².

Biotechnology Industry Research Assistance Council (BIRAC) is a not-for-profit Public Sector Enterprise, set up by Department of Biotechnology (DBT), Government of India as an Interface Agency to strengthen and empower the emerging Biotech enterprise to undertake strategic research and innovation, addressing nationally relevant product development needs. BIRAC is an industry-academia interface and implements its mandate through a wide range of impact initiatives, be it providing access to risk capital through targeted funding, technology transfer, IP management and handholding schemes that help bring innovation excellence to the biotech firms and make them globally competitive. BIRAC has initiated several schemes, networks and platforms that help to bridge the existing gaps in the industry-academia Innovation research and facilitate novel, high quality affordable products development through cutting edge technologies.



Source: www.birac.nic.in

¹⁷⁹<https://www.ijcmph.com/index.php/ijcmph/article/view/906>

¹⁸⁰<https://www.future-science.com/doi/10.4155/fmc.15.47>

¹⁸¹<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5725781/#B4>

¹⁸²<https://www.sciencedirect.com/science/article/pii/S0970389617305384>

BIRAC has initiated partnerships with several national and global partners to collaborate, stimulate, foster and enhance the strategic research and innovation capabilities of the Indian biotech industry, particularly start-ups and SME's, for creation of affordable products addressing the needs of the largest section of society. The key strategies of BIRAC are to foster innovation and entrepreneurship, promote affordable innovation in key social sectors, empowerment of start-ups & small and medium enterprises, contribute through partners for capability enhancement and diffusion of innovation, enable commercialization of discovery, ensure global competitiveness of Indian enterprises

Social Innovation Immersion Program (SIIP) of BIRAC is aimed at creating a pool of biotech "Social Innovators" who can identify needs & gaps within communities and then can help bridge the gaps either through an innovative product development or services. Social Innovation programme for Products: Affordable & Relevant to Societal Health (SPARSH) of BIRAC aims at promoting the development of innovative solutions to society's most pressing social problems. The scheme intends to create a pool of social innovators in the biotech arena who will identify the specific needs and gaps in healthcare. Financial and technical support is provided for developing market-based solutions that have potential to bring cost effective health care breakthroughs to vulnerable populations in particular.

India Knowledge Hub¹⁸³

NITI Aayog has created the India Knowledge Hub (IKH), a dynamic web portal, functioning as a repository to store and disseminate best practices from across the country.

The portal serves as a dynamic sharing platform in which the key functionaries can directly upload best practices for replication in other regions. While, mostly the best practices are directly uploaded by the district collectors from any State/UT, Departments of State governments and Central Ministry can also upload the best practices in the portal. In its first phase, the portal is also being extended to certain non-government institutions which have requested access to upload best practices. Presently, there are over 400 best practices that are catalogued in 20 thematic areas, covering Digital India, e-governance, law and order and security, financial inclusion, health, nutrition, education, Public Private Partnership (PPP) among others. The best practices are examples of the innovative practices adopted in districts. It also provides a platform for valuable feedback and is visible to the public.



Atal Innovation Mission¹⁸⁴

The Atal Innovation Mission (AIM) is a flagship initiative set up by the NITI Aayog to promote innovation and entrepreneurship across the length and breadth of the country, based on a detailed study and deliberations on innovation and entrepreneurial needs of India in the years ahead. It develops new policies and programmes for fostering innovation in different sectors of the economy and provide platform and collaboration opportunities to various stakeholders in the entrepreneurial space.



¹⁸³<http://indiaknowledgehub.gov.in/content/knowledgeportal/en/home.html>

¹⁸⁴<https://www.aim.gov.in/>

AIM is also envisaged as an umbrella innovation organization that would play an instrumental role in alignment of innovation policies between central, state and sectoral innovation schemes incentivizing the establishment and promotion of an ecosystem of innovation and entrepreneurship at various levels - higher secondary schools, science, engineering and higher academic institutions, and SME/MSME industry, corporate and NGO levels. Long term goals of AIM include establishment and promotion of Small Business Innovation Research and Development at a national scale (AIM SBIR) for the SME/MSME/startups, and in rejuvenating Science and Technology innovations in major research institutions of the country like CSIR (Council of Scientific Industrial Research), Agri Research (ICAR) and Medical Research (ICMR) aligned to national socio-economic needs.

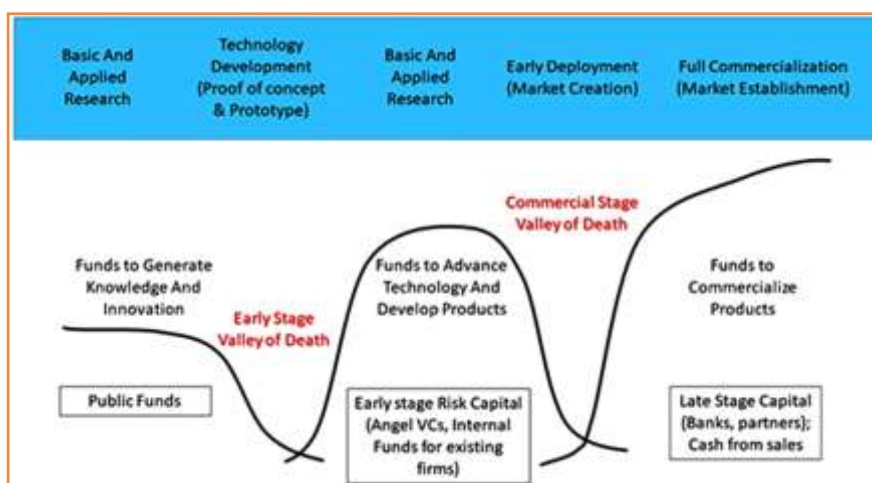
Atal Tinkering Labs – to promote creative, innovative mind set in schools

These ATLs are dedicated innovation workspaces of 1200-1500 square feet where do-it-yourself (DIY) kits on latest technologies like 3D Printers, Robotics, Internet of Things (IOT), Miniaturized electronics are installed using a grant of Rs 20 Lakhs from the government so that students from Grade VI to Grade XII can tinker with these technologies and learn to create innovative solutions using these technologies. To date, 2441 schools have already been selected for ATL Grants and by the end of 2018 over 5000 schools are expected to be operational.

Atal New India Challenge is an initiative by Atal Innovation Mission aimed at supporting innovators to create products/solutions based on advanced technologies in areas of national importance and social relevance through a grant-based mechanism. The vision of the Atal New India Challenge is two-fold:

- (a) help create products from existing technologies relevant for national and social causes (productization);
- (b) help new deep-tech products find markets and early customers (commercialization) in the context of India.

NITI Aayog’s Expert Committee on Innovation and Entrepreneurship (“Expert Committee”), had identified in its report the need to incentivize innovation in areas critical to India’s growth and development, such as health, housing, hygiene, energy and water. Researchers have long talked of the ‘Valleys of Death’ at the early stage and commercialization stage in taking innovations to market. The Atal New India Challenge aims to address the second Commercialization Valley of Death, in which innovators are unable to access resources for piloting, testing, and market creation.



Source: <https://niti.gov.in/>

The first set of 17 Atal New India Challenges (ANIC) has been launched on April 26th, 2018. The successful applicants will get a grant of upto Rs 1 crore for Atal New India Challenges and larger grants of upto Rs 30 crores for Atal Grand Challenges.

Atal Incubators – to promote entrepreneurship in universities and industry

At the university, NGO, SME and Corporate industry levels, AIM is setting up world-class Atal Incubators (AICs) that would trigger and enable successful growth of sustainable startups in every sector /state of the country. Women led incubators and entrepreneurial startups are strongly encouraged by AIM. AIM is providing a grant of upto Rs 10 crores to successful applicants for setting up greenfield incubators or scaling up existing ones. To date 19 Atal Incubators have been selected. Before the end of 2018-19, we would have 50+ Atal Incubators operational.

XIV. Re-purposing of Medicines for Reduced Approval Timeframe, Decreased Costs and Making use of Existing data: Potential of Scalability of NIH Model

Drug repurposing/ repositioning is an unconventional drug discovery approach to explore new therapeutic benefits of existing, shelved and the drugs in clinical trials. This approach is currently emerging to overcome the bottleneck constraints faced during traditional drug discovery in respect of financial support, timeline and resources. Traditional drug development process consumes time and resources immensely before a molecule is labored into the open market. Despite huge investments, the chances of a lead molecule to enter open market are often minimal. The itinerary of the research molecule remains unpredictable, throughout its lifecycle. This situation makes newer pharma companies to give upon dreams on novel drug discovery. One of the viable options for newcomers in the field of new drug research is drug repurposing.¹⁸⁵



Therapeutic development is a costly, complex and time consuming process. The average length of time from target discovery to approval of a new drug is about 14 years. The failure rate during this process exceeds 95 percent, and the cost per successful drug can be \$1 billion or more. The high therapeutic development failure rate means there are many existing, partially developed therapeutic candidates that could be repurposed for use in new disease indications.

The process of finding new uses of existing drugs (marketed drugs and failed or idle compounds) outside the scope of the original indication is variously referred as repositioning, redirecting, repurposing, and reproofing. Various techniques including data mining, bioinformatics, and usage of novel screening platforms have been used for identification and screening of potential repositioning candidates. However, challenges in clinical trials and intellectual property issues may be encountered during the repositioning process. Nevertheless, such initiatives not only add value to the portfolio of pharmaceutical companies but also provide an opportunity for academia and government laboratories to develop new and innovative uses of existing drugs for infectious and neglected diseases, especially in emerging countries like India.¹⁸⁶

The repositioning or “repurposing” of existing therapies for alternative disease indications is an attractive approach that can save significant investments of time and money during drug development.

Repositioned drugs have the advantage of decreased development costs and decreased time to market than traditional discovery efforts, due to availability of previously collected pharmacokinetic, toxicology, and safety data. In fact, this strategy of using existing therapeutics for new indications has demonstrated success through previous observational studies and serendipity, such as sildenafil (Viagra), a phosphodiesterase inhibitor initially developed to treat

¹⁸⁵<https://www.sciencedirect.com/science/article/pii/S0753332218372871>

¹⁸⁶<http://www.jpgmonline.com/article.asp?issn=0022-3859;year=2011;volume=57;issue=2;spage=153;epage=160;aulast=Padhy>

angina and now repurposed as a medication for erectile dysfunction, as well as metformin (Glucophage), a common diabetes medication that is now the active chemical in 100+ ongoing Phase II and Phase III clinical trials as a cancer therapeutic¹⁸⁷. Other examples include plerixafor, studied as an inhibitor of HIV but subsequently launched in 2009 for mobilization of hematopoietic stem cells in the treatment of multiple myeloma, and milnacipran, initially developed and launched outside the US as an antidepressant and later approved in the US for the treatment of fibromyalgia in 2009. Bupropion, originally used for depression, was repurposed for smoking cessation; and thalidomide, once a treatment for morning sickness, is now used for multiple myeloma.¹⁸⁸

Existing drugs that are either approved or have been shown to be safe in late-stage trials, but have failed to meet end points of their originally-targeted indications, can leverage their inherently reduced development risk into potentially new indications. According to a recent report based on a survey of 30 pharmaceutical and biotechnology firms, the cost to relaunch a repositioned drug averages \$8.4 million, whereas to relaunch a new formulation of an existing drug in its original indication costs an average \$41.3 million. In both cases, the drug has reached the market.¹⁸⁹

Role of US FDA/ EMA in approvals in Repurposing of drugs

In the US, there are three separate regulatory approval pathways that allow for the registration of distinct classifications of drugs, as outlined in the Food, Drug and Cosmetics Act, although only one of these [i.e., “505(b)(2)”], is relevant to drug repurposing. All drug candidates for repurposing must be submitted through Section 505 (b) (2), regardless of whether it is for cancer therapeutics or alternate diseases. Section 505(b) (2) became available in 1984 under the Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Amendments). Such efforts can offer temporary protection for: i) new molecular entities, NMEs; ii) new dosage forms; iii) new administration routes; iv) new indications; and v) new NME combinations.

In Europe, a parallel approval pathway is regulated by the EMA under Article 10 of Directive 2001/83/EC. However, in contrast to section 505(b) (2) of the Food, Drug and Cosmetics Act, which allows the use of non-proprietary studies that have previously achieved a high standard of quality and safety to support any part of an application.

National Institute of Health Model

The National Center for Advancing Translational Sciences (NCATS) Discovering New Therapeutic Uses for Existing Molecules (New Therapeutic Uses) program at the National Institutes of Health (NIH) essentially serves as a “matchmaker” to provide academic investigators an unprecedented opportunity to access pharmaceutical industry agents and explore new ways to treat disease. Launched in 2012 as a pilot initiative, the New Therapeutic Uses approach could produce new treatments for patients more quickly than starting from scratch. To facilitate the required public-private partnerships, NCATS uses template agreements to help streamline legal and administrative processes needed for research collaborations across multiple organizations. The agreements already have reduced time, cost and effort and enabled greater participation than traditional partnerships. For example, during the pilot program, the templates helped shorten the time required to establish collaborations to about three months instead of the more typical nine months to one year¹⁹⁰.

¹⁸⁷<https://www.ncbi.nlm.nih.gov/pubmed/25333032>

¹⁸⁸<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5963941/>

¹⁸⁹http://www.pharmatimes.com/news/drug_relaunch_strategies_hit_the_jackpot_989888

¹⁹⁰<https://ncats.nih.gov/files/NTU-factsheet.pdf>

NCATS provides governmental financial support for drug repurposing to aid in the generation and implementation of novel therapeutics. NCATS has dedicated resources for drug repurposing efforts. Additionally, the Center's scientists conduct research in high-throughput assay development and screening, informatics and modeling, and analytical and medicinal chemistry to improve the repurposing process.

Early-Stage Repurposing: A common first step in repurposing is to screen libraries of already approved compounds against a disease-specific biological assay. From such screens, researchers can select a subset of bioactive compounds for further investigation and development in secondary and tertiary assays evaluating relevant aspects of disease biology and molecular pathophysiology.

Late-Stage Repurposing: Post identification of promising approved or existing molecule through initial screening and validation, NIH experts aid further clinical investigators by supporting the development of regulatory-quality data packages, which enable the drug's entry into clinical trials for the new disease indication.

The launch of two major initiatives in the US, Clinical and Translational Science Award (CTSA), which supports clinical and translational research, and the Molecular Libraries Program which supports primarily research in chemical probe development; as well as a complementary initiative in Europe, the Innovative Medicines Initiative, IMI— which fosters joint projects between academic and pharmaceutical research units; and last but not least the increasing amount of public and open source data, knowledge and software that can be utilized for drug repurposing projects.

These changes have been accelerated by NIH programs that support drug discovery and development as well as clinical trials such as the National Cancer Institute's Experimental Therapeutics Program (NExT¹⁹¹) and the NIH Rapid Access to Therapeutic Development Program (RAID to be re-launched as (BRIDGS¹⁹²) which has led several institutions to collect, use, and report on approved drugs to make available collections of molecules that have been previously used in clinical trials (NIH Clinical Collections¹⁹³) for repurposing.

The CTSA Pharmaceutical Assets Portal: The CTSA Pharmaceutical Assets Portal project was initiated by the consortium of universities linked by the Clinical and Translational Science Award (CTSA). The drug rescue and repurposing project is part of the National Center for Advancing Translational Sciences (NCATS). They are making comprehensive and conscious efforts to identify appropriate abandoned compounds and potential partners, and making data and resources available to the pharma industry.

NIH's Therapeutics for Rare and Neglected Diseases TRNDs (TRND) and NCATS Chemical Genomics Center (NCGC) has created the NCGC Pharmaceutical Collection (NPC) program. This is an ongoing project for NIH and is expected to benefit drug development communities via the NPC Informatics Resource browser. NPC has the collection of more than 9000 drugs and drug-like compounds, which represent the repurposing compounds space, along with more than 200 assays for drug targets. They provide not only the possibility of rapid therapeutic advances but also provide new lead or probe development.

¹⁹¹<http://next.cancer.gov/default.htm>

¹⁹²<http://nctt.nih.gov/bridgs/>

¹⁹³<http://nctt.nih.gov/now>

Table 1: Examples of repositioned drugs (this list is neither extensive nor exhaustive)¹⁹⁴

Drug	Original Indication	New Indication
Allopurinol	Cancer	Gout
Amantadine	Influenza	Parkinson's disease
Amphotericin	Antifungal	Leishmaniasis
Arsenic	Syphilis	Leukemia
Aspirin	Inflammation, pain	Antiplatelet
Atomoxetine	Depressive disorder	ADHD
Bimatoprost	Glaucoma	Promoting eyelash growth
Bromocriptine	Parkinson's disease	Diabetes mellitus
Bupropion	Depression	Smoking cessation
Colchicine	Gout	Recurrent pericarditis
Colesevelam	Hyperlipidemia	Type 2 diabetes mellitus
Dapsone	Leprosy	Malaria
Disulfiram	Alcoholism	Melanoma
Doxepin	Depressive disorder	Antipruritic
Eflornithine	Depression	ADHD
Finasteride	Benign prostatic hyperplasia	Male pattern baldness
Gabapentin	Epilepsy	Neuropathic pain
Gemcitabine	Antiviral	Cancer
Lomitapide	Lipidemia	Familial hypercholesterolemia
Methotrexate	Cancer	Psoriasis, rheumatoid arthritis
Miltefosine	Cancer	Visceral leishmaniasis
Minoxidil	Hypertension	Hair loss
Naltrexone	Opioid addiction	Alcohol withdrawal
Naproxen	Inflammation, pain	Alzheimer's disease
Nortriptyline	Depression	Neuropathic pain
Premetrexed	Mesothelioma	Lung cancer
Propranolol	Hypertension	Migraine prophylaxis
Raloxifene	Contraceptive	Osteoporosis
Sildenafil	Angina	Erectile dysfunction; pulmonary hypertension
Thalidomide	Morning sickness	Leprosy; multiple myeloma
Tretinoin	Acne	Leukemia
Zidovudine	Cancer	HIV/AIDS
Zileuton	Asthma	Acne

¹⁹⁴<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6027196/#B11-pharmaceuticals-11-00057>⁹<https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/drug-repositioning>

XV. Patent Landscaping of Health Products (WHA 72.17/2019)

The adoption of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) in the WTO almost 25 years earlier is continuing to influence access to medicines and medical products.

The World Trade Organisation (WTO) deals with the rules of trade between nations at a near-global level; responsible for negotiating and implementing new trade agreements; and in charge of policing member countries' adherence to all the WTO agreements, signed by the majority of the world's trading nations and ratified in their parliaments. WTO is mandated to review the national trade policies and to ensure the coherence and transparency of trade policies through surveillance in global economic policy making¹⁹⁵.

With the implementation of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS in 1994), Intellectual Property Rights (IPRs) on the part of WTO member states, are obligations of commercial policy that require compliance. Adoption and enforcement of at least the minimum standards will procure considerably stronger global protection of intellectual assets¹⁹⁶. TRIPS, the first international agreement to mandate nations to provide “minimum” standards of IP protection, which resulted in countries to retain some domestic discretion to tailor intellectual property rights in accordance with their policy preferences¹⁹⁷.

Articles 7 and 8 of TRIPS Agreement or the subsequent Doha Public Health Declaration are designed to promote interpretations that foster public health. In addition, newer free trade agreements with investment chapters typically have an IP chapter that has even stronger IP protections than TRIPS which enables an intrusion onto TRIPS flexibilities. Modest strategies are required to counter regime shifting of IP enforcement to ensure the bona fide authority of governments to protect public health by defining and clarifying key terms to minimize harm to domestic sovereignty and TRIPS flexibilities¹⁹⁸.

Flexibilities under the TRIPS (Trade-Related Aspects of Intellectual Property Rights) agreement allow countries to gain access to medicines that in other countries may still be under patent, in the interest of public health. Equitable access to essential, high-quality and affordable essential medicines and other medical technologies depends on affordable and fair pricing and effective financing schemes. Promoting affordable and fair prices and cost-effective interventions is central to the achievement of universal health coverage¹⁹⁹.

There is a need to increase synthesis of intellectual property and trade rules, and use of TRIPS flexibilities to expand access to new therapies. Many World Health Assembly resolutions in WHO have requested WHO to address the impact of trade agreements and intellectual property protection on public health and access to health products.

¹⁹⁵https://saylordotorg.github.io/text_fundamentals-of-global-strategy/s13-02-regulation-of-international-tr.html

¹⁹⁶<https://www.piie.com/publications/working-papers/regulatory-standards-wto>

¹⁹⁷ 18 MNJLST 427 : regime shifting of ip lawmaking and enforcement from the wto to the international investment regime

¹⁹⁸ 18 MNJLST 427 : regime shifting of ip lawmaking and enforcement from the wto to the international investment regime

¹⁹⁹<https://www.who.int/medicines/areas/access/en/>

The Global strategy and plan of action on public health, innovation and intellectual property (World Health Assembly resolution WHA61.21), along with other relevant resolutions, constitutes the basic mandate for WHO's work in this area. WHO's Global Strategy and Plan of Action also identified the need to improve access to patent information to facilitate the determination of the patent status of health products. It urges stakeholders to:

- Facilitate access to user-friendly global databases which contain public information on the administrative status of health-related patents. This includes supporting existing efforts for determining the patent status of health products, and to
- Promote further development of such global databases including, if necessary, compiling, maintaining and updating such global databases.

As a direct result of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property of 2008 (WHA61.21), UNITAID established an Medicines Patent Pool (MPP), a United Nations-backed organization for HIV medicines in 2010. Access to affordable generic medicines can be achieved through licensing agreements. The MPP initially focused on patents related to HIV medicines to promote low-cost generic production and the development of fixed-dose combinations and paediatric formulations. The MPP has expanded its mandate to cover hepatitis C and tuberculosis.

The rationale for having patents is to make investment in innovation attractive and to offer a mechanism which ensures that the knowledge contained in the patent application is accessible to society. Among others, the obligation of patent owners to publicly disclose their inventions enables society to know, and eventually use, the knowledge contained in patent documents. However, the use of the exclusive right can itself contribute to a market distortion and can lead to a situation characterized by inefficiencies, high prices and the under provision of goods.

Patents present substantial challenges to medicines availability. However, TRIPS flexibilities in patent law have been used by a number of countries to secure access to generic medicines. The most frequently deployed flexibilities are compulsory licensing of medicines, government use of patents, and the waiver that allows LDCs to postpone granting or enforcing medicines patents and test data protection until 2033. These options have been used more widely than is usually assumed. New figures show that since 2001, there have been 34 instances of compulsory licensing (CL) of medicines by 24 countries, 51 instances of government use of patents by 35 countries, and 32 of non-enforcement of patents by 24 World Trade Organization LDC Members. The peak of these instances falls between 2004 and 2008, coinciding with increased global funding for HIV. Although originally focused on HIV, 23 out of 85 total instances of CL and government use have concerned non-HIV medicines, including seven instances for cancer medicines between 2008 and 2014, of which five were granted. These measures have improved access to medicines. For example, in Thailand, CLs for erlotinib, docetaxel, letrozole, and clopidogrel save the health-care system \$142 million per year. In the past decade and a half, some countries have amended their patent laws to reflect health concerns. For example, India rewards innovation but prevents trivial patents and so-called ever-greening of patents.

Patent landscaping can potentially assist the generic industry, researchers, government and policy makers, by facilitating generic industry and thereby promoting competition. Although patents require publication, determining patent status of medicines can be extraordinarily difficult. Additionally, patent landscapes may be contained within bilateral commercial licenses, these licenses are not publicly accessible. Thus, it is an enormous advantage that the MPP has succeeded in requiring originators to disclose the patents that are pending or granted in licensed

territories²⁰⁰. This information is helpful to advocates, countries, and generic producers weighing options to pursue generic competition in non-licensed territories, whether by permitted extra-territorial sales or via compulsory or government-use licenses.

Patent landscape provides a snapshot of the patent situation of a specific technology, either within a given country or region, or globally. They can inform policy discussions, strategic research planning or technology transfer. They may also be used to analyze the validity of patents based on data about their legal status²⁰¹. As a result of generic industry penetration, prices of medicines will come down promoting affordability and access.

As mandate by WHA61.21, WHO has intensified its collaboration with other relevant international organizations, in particular through trilateral collaboration with WIPO and WTO, as well as with other organizations, including UNCTAD and UNDP. Trilateral cooperation with WIPO and WTO is fostering a better understanding of the linkage between public health and intellectual property policies and enhancing a mutually supportive implementation of those policies (Access to medicines and vaccines 4 April 2019 - WHA72.17) .

The patent system discloses²⁰²:

- Legal information, including published details of what material is patented, with what legal scope, in what countries, in whose name, and when it passes into the public domain;
- Technological information, such as a patent's so-called 'teaching' or technical disclosure, which is required to give a skilled reader all the information needed to put the new technology into practical effect.



²⁰⁰<https://www.medspal.org/?page=1>

²⁰¹https://www.wipo.int/patentscope/en/programs/patent_landscapes/

²⁰²https://www.wipo.int/wipo_magazine/en/2008/04/article_0005.html

XVI. Access Strategies, Patent Pool Mechanisms and Licensing for Medical Products and Health Technologies Including the Role of Pharmaceutical Sector

Improving access to medical products has been a central focus of global health efforts over the past two decades. Apart from community mobilisation and competition law challenges, many global initiatives aim to broaden access to health technologies by improving the public health²⁰³.

The countries are burdened with diseases relating to communicable diseases (CDs), non-communicable diseases (NCDs) and the risk of new diseases²⁰⁴. Access to medicines is critical for health outcomes. Policies and approaches for the pricing and procurement of health technologies are vital to ensure the availability and affordability of essential medicines and health products for their populations²⁰⁵. Many medical products (i.e., drugs, vaccines, and diagnostics) are unaffordable to the populations in need, one of the battling factors in the developed and developing economies²⁰⁶.

Access to medicines depends on multiple factors like use of drugs, adequate and sustainable financing, affordable prices and reliable supply systems. In developed countries, expenditure on pharmaceuticals for the population is largely publicly funded through reimbursement and insurance schemes, while in developing countries, typically, the cost of 50–95% of drugs are out-of-pocket expenditure by the patients themselves. The 2001 Doha Declaration on TRIPS and Public Health signed by all WTO



Member States noted that intellectual property protection was important for the development of new medicines, and also recognized the concerns about its effects on prices²⁰⁷.

Public health and Intellectual Property rights go hand in hand in terms of innovation in treatments and development of medications. The legal structures such as patents are designed in a way to encourage innovation and to offer a system which ensures the benefits accessible to the society²⁰⁸.

The inclusion of universal health coverage (UHC) in the Sustainable Development Goals has led to countries focusing to build health systems that provide access to high-quality essential health care services; safe, effective, and affordable essential medicines and vaccines for all; as well as financial risk protection²⁰⁹ (SDG target 3.8).

²⁰³<https://pdfs.semanticscholar.org/8f64/028dd8d2e50b6a36005fbf35e6719203ed70.pdf>

²⁰⁴<https://apps.who.int/iris/bitstream/handle/10665/312273/WHO-NMH-NMA-GCM-18.12-eng.pdf>

²⁰⁵<http://www.asia-pacific.undp.org/content/rbap/en/home/presscenter/articles/2019/improving-pricing-and-procurement-of-health-technologies-to-adva.html>

²⁰⁶<https://www.ncbi.nlm.nih.gov/pubmed/28099819/>

²⁰⁷<https://apps.who.int/iris/bitstream/handle/10665/258915/TRIPS.pdf?sequence=1&isAllowed=y>

²⁰⁸<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3217699/> : IPR: An overview and implications in pharmaceutical industry

²⁰⁹https://iris.wpro.who.int/bitstream/handle/10665.1/12880/sdg_poster_goal3_3.8_eng.pdf

In this context, access to medical products is ensured by:

- Parallel importation that allows for importation of the patented product from a third country where it is sold at a lower price.
- Out-licensing which could be implemented as long as the terms and conditions are clearly defined which includes medicine, country of sale, production, enforcement measures, rights granted to the manufacturer and royalties to be paid.
- Compulsory license, issued by a competent public authority, to use a patented invention without the authorization of the patent holder which can be used to authorize the import, production and sale of a generic version of a patented product before relevant patents expire.
- Voluntary licensing (VL) that authorizes a generic manufacturer to distribute a patented medicine in certain countries and it is a strategy to increase access to medicines by facilitating low-cost production of medicines for low-income populations²¹⁰.
- A government use authorization can be considered as a special case of compulsory licensing, i.e. when the government issues compulsory license for its own purposes, for instance to ensure the availability of medicines in public health facilities. The TRIPS Agreement allows countries to issue compulsory licenses (including government use authorizations), and leaves countries free to decide the grounds, or reasons, for issuing a compulsory license²¹¹.

At the Sixty-first World Health Assembly in 2008, the World Health Organization (WHO) called to “examine the feasibility of voluntary patent pools to promote innovation of and access to health products and medical devices²¹².” At this time, patent pools in public health did not exist. New, safe and effective patented therapies were out of reach of LMICs’ populations. While the concept of patent pools was not certain that such a model could effectively accelerate access to treatment²¹³.

Medicines Patent Pool (MPP) established by UNITAID seems to have provided countries with an efficient alternative. Pools in general facilitate the licensing agreements for sharing of data and expertise under concrete terms and conditions between originators and generic manufacturers for the production of antiretrovirals for hepatitis C, HIV and tuberculosis²¹⁴.

It has been stated that pharmaceutical companies must take seriously their baseline responsibility to respect the right to health and comply with the provisions contained in national patent laws that are designed to facilitate access to medicines²¹⁵. Certain new licensing arrangements have evolved where voluntary licensing has been promoted. E.g. for tackling Hepatitis C. The originator companies Gilead and Bristol Myers Squibb (BMS) have signed voluntary license agreements with Indian drug companies that enable producers to manufacture and/or sell generic versions of sofosbuvir, ledipasvir, velpatasvir (Gilead) and daclatasvir (BMS) in countries listed in the agreements (“the territory” of the license). Consequently, all countries that are included in these agreements can procure generic Direct Acting Antivirals (DAAs) from the licensees at generally more affordable prices²¹⁶.

²¹⁰<https://www.orfonline.org/wp-content/uploads/2016/04/Special-Report-11-Tanoubi-Ngangom.pdf>

²¹¹<https://apps.who.int/iris/bitstream/handle/10665/272976/Public-health-protection.pdf?sequence=1&isAllowed=y>

²¹²http://www.wpro.who.int/health_research/wha61_21_global_strategy_poa_health_innovation_may2008.pdf

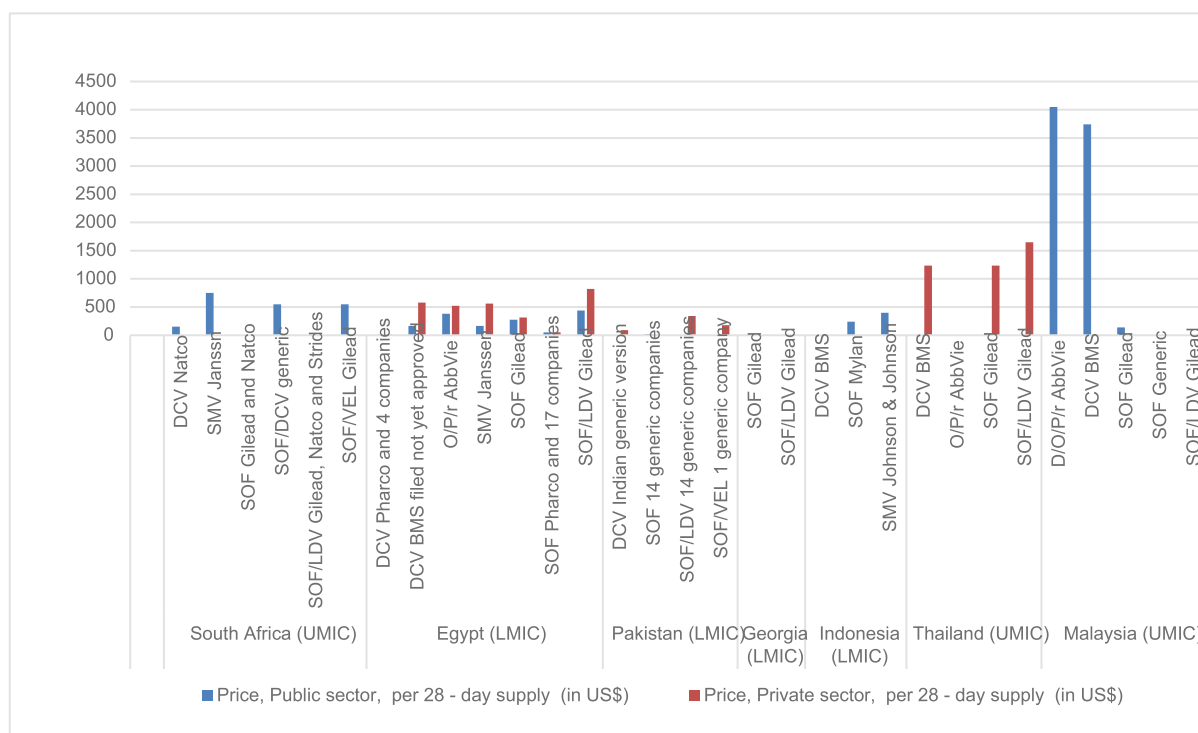
²¹³<https://medicinespatentpool.org/mpp-media-post/public-health-licensing-to-increase-access-and-facilitate-innovation-the-medicines-patent-pool-model/>

²¹⁴The never-ending story of access to medicines: W.I.P.O.J. 2016, 8(1), 54-63

²¹⁵Defining the right to health responsibilities of patent-owning pharmaceutical companies: I.P.Q. 2019, 1, 43-60

²¹⁶<https://apps.who.int/iris/bitstream/handle/10665/260445/WHO-CDS-HIV-18.4-eng.pdf;jsessionid=154971AA2306949A28A9D7F2C0ACBBA2?sequence=1>

Summary of DAA procurement situation in countries, mid-2017²¹⁷



BMS: Bristol-Myers Squibb; DAA: direct-acting antiviral; DCV: daclatasvir; D/O/P/r: daclatasvir + ombitasvir/paritaprevir/ritonavir; HCV: hepatitis C virus; LDV: ledipasvir; LIC: low-income country; LMIC: lower-middle-income country; O/P/r: ombitasvir/paritaprevir/ritonavir; SOF: sofosbuvir; UMIC: uppermiddle-income country; VEL: velpatasvir

In 2005, India was the first country to incorporate a provision in its law that specifically aimed at preventing the grant of “evergreening” patents. The Indian law also allows for pre- and post-grant patent oppositions. Public interest groups in India have successfully used these provisions to oppose patent applications on several medicines of public health importance, including the following ARVs: nevirapine hemihydrate, tenofovir, abacavir, ritonavir, and the combination of lopinavir and ritonavir, among others²¹⁸.

²¹⁷<https://apps.who.int/iris/bitstream/handle/10665/260445/WHO-CDS-HIV-18.4-eng.pdf;jsessionid=154971AA2306949A28A9D7F2C0ACBBA2?sequence=1>

²¹⁸<https://apps.who.int/iris/bitstream/handle/10665/272977/Country-experiences-TRIPS-Part1.pdf?sequence=1&isAllowed=y>

XVII. Regulatory Approaches for Approval of Pharma & Biosimilar Drugs, and Gene and Cell Therapies - USFDA, EMA Models

A biosimilar drug is defined in the US Food and Drug Administration (FDA) guidance document as a biopharmaceutical that is highly similar to an already licensed biologic product (referred to as the reference product) notwithstanding minor differences in clinically inactive components and for which there are no clinically meaningful differences in purity, potency, and safety between the two products. The development of biosimilars is a challenging, multistep process. Typically, the assessment of similarity involves comprehensive structural and functional characterization throughout the development of the biosimilar in an iterative manner and, if required by the local regulatory authority, an in vivo nonclinical evaluation, all conducted with direct comparison to the reference product²¹⁹.

The US Food and Drug Administration approves biosimilar products and provides the scientific and regulatory advice needed to bring safe and effective biosimilars to market. The approval of biosimilar products can improve access to care for patients by increasing the number of medication options and potentially lower costs²²⁰. All biosimilar and interchangeable products meet FDA's rigorous standards for approval for the indications (medical conditions) described in product labeling. Once a biosimilar has been approved by FDA, patients and health care providers can be assured of the safety and effectiveness of these products, just as they would for the reference product²²¹.

The European Medicines Agency (EMA) and the United States (US) Food and Drug Administration (FDA) guidance documents stipulate that a biosimilar manufacturer must perform a series of extensive similarity assessments in order to demonstrate biosimilarity to the reference product, and to ultimately gain regulatory approval or licensure. The World Health Organization (WHO) has also published general guiding principles for the development of biosimilars, with the aim of providing a coherent approach for national regulatory guidelines²²².

With the objective of ensuring patient safety, USFDA provides 'MedWatch Safety Alerts' which include timely new safety information on human drugs, medical devices, vaccines and other biologics, dietary supplements, and cosmetics²²³. The alerts contain actionable information that may impact both treatment and diagnostic choices for healthcare professionals and patients. Further, the Sentinel Initiative of USFDA enhances its ability to proactively monitor the safety of medical products after they have reached the market²²⁴. Through Sentinel, the FDA can rapidly and securely access information from large amounts of electronic healthcare data, such as electronic health records (EHR), insurance claims data and registries, from a diverse group of data partners. Sentinel uses a distributed data approach which allows the FDA to monitor the safety of regulated medical products, while securing and safeguarding patient privacy.

²¹⁹<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5698755/>

²²⁰<https://www.fda.gov/drugs/biosimilars/biosimilar-product-information>

²²¹<https://www.medscape.com/viewarticle/863411>

²²²<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5698755/>

²²³<https://www.fda.gov/safety/medical-product-safety-information/medwatch-safety-alerts-human-medical-products>

²²⁴<https://www.fda.gov/safety/fdas-sentinel-initiative>

The USFDA also conducts economic analyses of all its proposed and final regulations. Each economic analysis includes an assessment of the costs, benefits, and cost-effectiveness of the action, as well as of the most promising alternative actions. The information on incremental costs and benefits helps FDA to decide on the best mode to deal with a public health problem²²⁵.

The ultimate goal of the regulatory bodies is to ensure that biosimilars meet high standards of quality, safety, and efficacy, and are highly similar to the reference product. There are many regulatory guidance documents, there is no global consensus on the regulatory approval pathway for biosimilars²²⁶.

The Center for Biologics Evaluation and Research (CBER) regulates cellular therapy products, human gene therapy products, and certain devices related to cell and gene therapy. CBER uses both the Public Health Service Act and the Federal Food Drug and Cosmetic Act as enabling statutes for oversight. Cellular therapy products include cellular immunotherapies, cancer vaccines, and other types of both autologous and allogeneic cells for certain therapeutic indications, including hematopoietic stem cells and adult and embryonic stem cells. In addition to regulatory oversight of clinical studies, CBER provides proactive scientific and regulatory advice to medical researchers and manufacturers in the area of novel product development²²⁷.

The new digital health approach of the USFDA is further aiming to provide new regulatory pathways for the pharmaceutical sector.²²⁸ In view of this approach, USA is considering a legislation that would overhaul the manner in which OTC drugs are approved, shifting to a system in which products would be approved based on administrative orders instead of through a notice-and-comment rulemaking process²²⁹. This could significantly shorten the regulatory review process, and, paired with the digital health component, create new opportunities for companies to get new OTC drugs to market more quickly.

The European Medicines Agency (EMA) evaluates biological medicines produced using biotechnology including biosimilar medicines, before they can be approved and marketed in the EU. The authorisation of biosimilar medicines in the EU requires a different set of data compared to other biological medicines. However, the same high standards of quality, safety and efficacy are applied. As for any medicine, the benefits of a biosimilar medicine have to be shown to outweigh its risks before it is approved for marketing. This requires large amounts of data, including data on its purity and manufacture, how well the biosimilar medicine works and extensive comparison with the reference medicine. The comparisons are carried out in a step-wise fashion that begins with detailed studies in the laboratory comparing the structure with the function of the medicines, then moves on to comparative clinical studies (studies in humans) as necessary. Following positive assessment by EMA, biosimilar medicines are approved by the European Commission for use in EU patients²³⁰.

Advanced therapy medicinal products²³¹ (ATMPs) are medicines for human use that are based on genes, tissues or cells. They offer groundbreaking new opportunities for the treatment of disease and injury. All advanced therapy medicines are authorised centrally via the European Medicines Agency (EMA). They benefit from a single evaluation and authorisation procedure. As

²²⁵<https://www.fda.gov/about-fda/reports/economic-impact-analyses-fda-regulations>

²²⁶<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5698755/#bit26438-bib-0026>

²²⁷<https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products>

²²⁸<https://www.pwc.com/us/en/health-research-institute/assets/pwc-hri-acceleration-by-regulation-march-2019-report.pdf>

²²⁹<https://www.congress.gov/bill/115th-congress/house-bill/5333/text>

²³⁰<https://ec.europa.eu/docsroom/documents/20961/attachments/1/translations/en/renditions/native>

²³¹<https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapy-medicinal-products-overview>

with all medicines, the EMA continues to monitor the safety and efficacy of advanced therapy medicines after they are approved and marketed. EMA also gives scientific support to developers to help them design pharmacovigilance and risk management systems used to monitor the safety of these medicines.

Stem cells are naturally occurring cells in the body that have the ability to divide and produce a range of different cell types. The past few years have seen a dramatic increase in the level of knowledge about stem cells, and research and investment into their uses in medicines. Stem cells are categorised as ATMPs when these cells undergo substantial manipulation or are used for a different essential function. They can be somatic-cell therapy products or tissue-engineered products, depending on how the medicine works in the body. EMA follows research into the use of stem cells in medicines very closely and is responsible for assessing marketing authorisation applications for medicines containing stem cells²³².

New scientific progress in cellular and molecular biotechnology has led to the development of advanced therapies, such as gene therapy, somatic cell therapy, and tissue engineering. This nascent field of biomedicine offers new opportunities for the treatment of diseases and dysfunctions of the human body²³³.

²³²<https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0001:0033:en:PDF>

²³³https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2007_1394/reg_2007_1394_en.pdf

XVIII. National Regulation and International Agreements Including Pricing of Medical Products for Affordable Access

Access to medicines generally includes two distinct components, viz. availability and affordability²³⁴. The price of many medicines (i.e., drugs, vaccines, and diagnostics) is unaffordable to the majority of the population in need, especially in least-developed countries, but also increasingly in middle-income countries. Several innovative approaches, based on partnerships, intellectual property, and pricing, are used to stimulate innovation, promote healthcare delivery, and reduce global health disparities. No single approach suffices, and therefore stakeholders need to further engage in partnerships promoting knowledge and technology transfer in assuring essential medicines to be manufactured, authorized, and distributed in low- and middle-income countries (LMICs) in an effort of making them available at affordable and acceptable conditions²³⁵.

Access to biomedical research is a natural premise for access to health care. Besides the problems posed by the globalization of the IP regime, the strong connection between commercial and non-commercial interests causes specific concerns, being that this technological sector is crucial for health care's economic potentialities, but also for producing health-related goods²³⁶.

During the Uruguay Round of the WTO the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement was signed in 1994, the primary focus on IPR and access to medicines. IPR issues are also relevant to other multilateral and bilateral trade agreements. Overall, TRIPS and the IPR provisions of Free Trade Agreements (FTAs) have received tremendous support from developed countries as a result of pressure from their industries, but have received mixed responses from developing country ministers. The trade was regulated through bilateral treaties between two nations for regulating global trade²³⁷.

The Doha Declaration affirmed the importance of the “right to protect public health and, in particular, to promote access to medicines for all”, and affirmed “the right of WTO Members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose²³⁸.” In addition, the Doha Declaration clarified that each country has the right to define a national emergency for itself, and that epidemics of any disease can always qualify as national emergencies.

The Doha Declaration further clarified that compulsory licenses are permissible at any time during these national emergencies, even after a developing nation has fully adopted the TRIPS Agreement²³⁹. Finally, recognizing that compulsory licenses may not be feasible for least developed nations that lack resources to manufacture the drugs, the Doha Declaration provided the option of parallel importation, which allows nations to import certain amounts of pre-made pharmaceuticals in return for reasonable compensation. Usually, the pharmaceutical companies will be able to sell the drugs cheaper in poorer countries, and recover costs with higher prices in developed countries. Alternatively, third-party countries could apply for

²³⁴https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3394851

²³⁵<https://www.frontiersin.org/articles/10.3389/fmed.2017.00218/full>

²³⁶14 WfJBIP 126: Open Source Models in Biomedicine: Workable Complementary Flexibilities Within the Patent System?

²³⁷https://saylordotorg.github.io/text_fundamentals-of-global-strategy/s13-02-regulation-of-international-tr.html

²³⁸World Trade Organization, Ministerial Declaration of 14 November 2001, 4, WTO Doc. WT/MIN(01)/DEC/1, 41 ILM (2001), available https://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_e.pdf [hereinafter Doha Declaration].

²³⁹<http://www.who.int/trade/glossary/story070/en/>.

compulsory licenses, produce the biologic drugs, and provide them to least developed countries through parallel importation²⁴⁰.

The Declaration was unanimously signed by WTO delegates and stated “that the TRIPS Agreement does not and should not prevent members from taking measures to protect public health²⁴¹.” Brazil, India, and South Africa used TRIPS flexibilities in different ways to change their national patent regimes to become TRIPS compliant within the scope of the flexibilities of the TRIPS Agreement.

In India, National Pharmaceutical Pricing Authority (NPPA) was established under the Drugs (Prices Control) Order, 1995 and entrusted to fix or revise the prices of controlled bulk drugs and formulations and to enforce prices and availability of medicines in India. It has also been empowered with the task of recovering amounts overcharged by manufacturers for controlled drugs from the consumers, and it also monitors the prices of decontrolled drugs in order to keep them at reasonable levels²⁴².



The Pradhan Mantri Bharatiya Janaushadhi Pariyojana (PMBJP) was launched by the Department of Pharmaceuticals, with the objective of making available quality generic medicines at affordable prices to all. This Scheme comprises more than 900 drugs and 154 surgical and consumables at affordable prices in all therapeutic categories such as Anti-infectives, Anti-diabetics, Cardiovascular, Anti-cancers, Gastro intestinal medicines, etc. PMBJP Kendras across the country are providing generic medicines to people at affordable prices.

The Political Declaration on NCDs, adopted by the UN General Assembly in 2011, WHO published its Global Action Plan for the Prevention and Control of NCDs 2013–2020 (GAP), which was endorsed by the World Health Assembly in 2013²⁴³. The six objectives, are to strengthen health systems to improve prevention, detection, treatment and management of people with or at high risk for cardiovascular diseases, diabetes, chronic respiratory diseases, cancer and other NCDs. This objective includes improving patient access to affordable medicines to treat NCDs. To help achieve this, NCD medicines must be both available in facilities when needed and affordable, especially for those on low-incomes. The WHO recognised this and included in the Global Action Plan a target of 80% availability of affordable basic technologies and essential medicines, including generics, required to treat major NCDs in both public and private facilities by 2025²⁴⁴.

It is important that the public health community not detract attention from the importance of trade for nutrition, especially the importance of changes to bilateral trade and investment agreements and away from trading. These are imperative for public health community involvement in matters of trade and health²⁴⁵.

²⁴⁰<http://apps.who.int/medicinedocs/documents/s16743e/s16743e.pdf>.

²⁴¹http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm

²⁴²13 Chi.-Kent J. Intell. Prop. 402: Globalizing standard of patent protection in WTO law and policy options for the Idcs: the context of Bangladesh

²⁴³UN General Assembly. Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable diseases. https://www.who.int/nmh/events/un_ncd_summit2011/political_declaration_en.pdf

²⁴⁴<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0171284>

²⁴⁵<https://www.bmj.com/content/365/bmj.l2217>

Political Declaration of the High-level Meeting on Universal Health Coverage “Universal Health Coverage: Moving Together to Build a Healthier World”

We, Heads of State and Government and representatives of States and Governments, assembled at the United Nations on 23 September 2019, with a dedicated focus for the first time on universal health coverage, reaffirm that health is a precondition for and an outcome and indicator of the social, economic and environmental dimensions of sustainable development and the implementation of the 2030 Agenda for Sustainable Development, and strongly recommit to achieve universal health coverage by 2030, with a view to scaling up the global effort to build a healthier world for all, and in this regard we:

1. Reaffirm the right of every human being, without distinction of any kind, to the enjoyment of the highest attainable standard of physical and mental health;
2. Reaffirm General Assembly Resolution 70/1 of September 2015, entitled “Transforming our world: the 2030 Agenda for Sustainable Development”, stressing the need for a comprehensive and people-centered approach, with a view to leaving no one behind, reaching the furthest behind first, and the importance of health across all the goals and targets of the 2030 Agenda for Sustainable Development, which are integrated and indivisible;
3. Reaffirm General Assembly Resolution 69/313 of 27 July 2015 on the Addis Ababa Action Agenda of the Third International Conference on Financing for Development, which reaffirmed strong political commitment to address the challenge of financing and creating an enabling environment at all levels for sustainable development in the spirit of global partnership and solidarity;
4. Reaffirm the strong commitments made through the political declarations adopted at the High-level Meetings on ending AIDS, on tackling antimicrobial resistance, on ending tuberculosis, and on the prevention and control of non-communicable diseases, as well as the General Assembly resolutions entitled “Consolidating gains and accelerating efforts to control and eliminate malaria in developing countries, particularly in Africa, by 2030”;
5. Recognize that universal health coverage is fundamental for achieving the Sustainable Development Goals related not only to health and well-being, but also to eradicate poverty in all its forms and dimensions, ensure quality education, achieve gender equality and women’s empowerment, provide decent work and economic growth, reduce inequalities, ensure just, peaceful and inclusive societies and to build and foster partnerships, while reaching the goals and targets included throughout the 2030 Agenda for Sustainable Development is critical for the attainment of healthy lives and well-being for all, with a focus on health outcomes throughout the life course;
6. Recall World Health Assembly resolution WHA72.4 entitled “Preparation for the high-level meeting of the United Nations General Assembly on universal health coverage”;
7. Recognize that health is an investment in the human capital and social and economic development, towards the full realization of the human potential and significantly contributes to the promotion and protection of human rights and dignity as well as the empowerment of all people;
8. Recognize that universal health coverage implies that all people have access, without discrimination, to nationally determined sets of the needed promotive, preventive, curative, rehabilitative and palliative essential health services, and essential, safe, affordable, effective

and quality medicines and vaccines, while ensuring that the use of these services does not expose the users to financial hardship, with a special emphasis on the poor, vulnerable, and marginalized segments of the population;

9. Recognize the need for health systems that are strong, resilient, functional, well-governed, responsive, accountable, integrated, community-based, people-centred and capable of quality service delivery, supported by a competent health workforce, adequate health infrastructure, enabling legislative and regulatory frameworks as well as sufficient and sustainable funding;

10. Recognize the need to tackle health inequities and inequalities within and among countries through political commitment, policies and international cooperation including those that address social, economic and environmental and other determinants of health;

11. Recognize that action to achieve universal health coverage by 2030 is inadequate and that the level of progress and investment to date is insufficient to meet target 3.8 of the Sustainable Development Goals, and that the world has yet to fulfil its promise of implementing, at all levels, measures to address the health needs of all, noting that:

- a. at least half of the world's population lack access to essential health services, more than 800 million people bear the burden of catastrophic spending of at least 10% of their household income on health care, and out of pocket expenses drive almost 100 million people into poverty each year;
- b. at the current pace, up to one third of the world's population will remain underserved by 2030 and a measurable acceleration is urgently needed to reach the health-related targets of the SDGs by 2030;
- c. despite major health gains over the past decades, including increased life expectancy, the reduction of maternal and under-5 mortality rates, and successful campaigns against major diseases, challenges remain with regard to emerging and re-emerging diseases, non-communicable diseases, mental disorders and other mental health conditions as well as neurological disorders, communicable diseases including HIV/AIDS, Tuberculosis and malaria, antimicrobial resistance, noting that non-communicable diseases account for over 70% of all deaths in the age group 30-69;
- d. despite the progress achieved at the global level, many health systems are not sufficiently prepared to respond to the needs of the rapidly ageing population;
- e. the high prices for some health products, and inequitable access to such products within and among countries, as well as financial hardships associated with high prices of health products continue to impede progress towards achieving universal health coverage;

12. Reaffirm the importance of national ownership and the primary role and responsibility of governments at all levels to determine their own path towards achieving universal health coverage, in accordance with national contexts and priorities, and underscore the importance of political leadership for universal health coverage beyond the health sector in order to pursue whole-of government and whole-of-society approaches, as well as health-in-all-policies approaches, equity-based approaches and life-course approaches;

13. Recognize that primary health care brings people into first contact with the health system and is the most inclusive, effective and efficient approach to enhance people's physical and mental health, as well as social well-being, and that primary health care is the cornerstone of a sustainable health system for universal health coverage and health-related Sustainable Development Goals, as was declared in the Declaration of Alma-Ata and reaffirmed by the Declaration of Astana;

14. Recognize the fundamental importance of equity, social justice and social protection mechanisms as well as the elimination of the root causes of discrimination and stigma in health-care settings to ensure universal and equitable access to quality health services without financial hardship for all people, particularly for those who are vulnerable or in vulnerable situations;

15. Recognize the consequence of the adverse impact of climate change, natural disasters, extreme weather events as well as other environmental determinants of health, such as clean air, safe drinking water, sanitation, safe, sufficient and nutritious food and secure shelter, for health and in this regard underscore the need to foster health in climate change adaptation efforts, underlining that resilient and people-centered health systems are necessary to protect the health of all people, in particular those who are vulnerable or in vulnerable situations, particularly those living in small island developing states;

16. Recognize that food security and food safety, adequate nutrition and sustainable, resilient and diverse nutrition-sensitive food systems are important elements for healthier populations;

17. Note that the increasing number of complex emergencies is hindering the achievement of universal health coverage, and that coherent and inclusive approaches to safeguard universal health coverage in emergencies are essential, including through international cooperation, ensuring the continuum and provision of essential health services and public health functions, in line with humanitarian principles;

18. Recognize the need for a strong global, regional and national partnerships for Sustainable Development Goals, which engages all relevant stakeholders to collaboratively support the efforts of Member States to achieve health-related Sustainable Development Goals, including universal health coverage;

19. Recognize that the world spends 7.5 trillion USD on health, which is close to 10% of global GDP, but that the allocation of public and external funds on health worldwide is disproportionate, considering that:

- a. on average, one third of national health expenditure is covered by out of pocket expenses, while less than 40% of funding on primary health care is from public source in low- and middle-income countries;
- b. external funding represents less than 1% of global health expenditure and there are important funding gaps given existing health needs, whereas low-income countries still rely on aid, which accounts for about 30% of national health spending;

20. Recognize that people's engagement, particularly of women and girls, families and communities, and the inclusion of all relevant stakeholders is one of the core components of health system governance, to fully empower all people in improving and protecting their own health, giving due regard to addressing and managing conflicts of interest and undue influence, contributing to the achievement of universal health coverage for all, with a focus on health outcomes;

21. Recognize the vital importance of strengthening legislative and regulatory frameworks and institutions for the achievement of universal health coverage;

22. Recognize that fighting corruption at all levels and in all its forms is a priority and that corruption is a serious barrier to effective resource mobilization and allocation and diverts resources away from activities that are vital for poverty eradication and sustainable development, which may undermine efforts to achieve universal health coverage;

23. Express concern of the global shortfall of 18 million health workers, primarily in low- and middle-income countries, and recognize the need to train, build and retain a skilled health workforce, including nurses, midwives and community health workers, who are an important element of strong and resilient health systems, and further recognize that increased investment in a more effective and socially accountable health workforce can unleash significant socio-economic gains and contribute to the eradication of poverty in all its forms and dimensions, empowerment of all women and girls and reduction of inequality;

We therefore commit to scale up our efforts and further implement the following actions:

24. Accelerate efforts towards the achievement of universal health coverage by 2030 to ensure healthy lives and promote well-being for all throughout the life course, and in this regard reemphasize our resolve to:

- a. progressively cover one billion additional people by 2023 with quality essential health services and quality, safe, effective, affordable and essential medicines, vaccines, diagnostics and health technologies, with a view to cover all people by 2030;
- b. stop the rise and reverse the trend of catastrophic out-of-pocket health expenditure by providing measures to assure financial risk protection and eliminate impoverishment due to health-related expenses by 2030, with special emphasis on the poor as well as those who are vulnerable or in vulnerable situations;

25. Implement most effective, high impact, quality-assured, people-centred, gender- and disability- responsive, and evidence-based interventions to meet the health needs of all throughout the life course, and in particular those who are vulnerable or in vulnerable situations, ensuring universal access to nationally determined sets of integrated quality health services at all levels of care for the prevention, diagnosis, treatment and care in a timely manner;

26. Implement high impact policies to protect people's health and comprehensively address social, economic and environmental and other determinants of health by working across all sectors through a whole-of-government and health-in-all-policies approach;

27. Prioritize health promotion and disease prevention, through public health policies, good governance of health systems, education, health communication and health literacy, as well as safe, healthy and resilient cities, enabling people, throughout their life course, including, among others, adolescents, to have increased knowledge to take informed health decisions and improve health-seeking behaviour;

28. Take multi-sectoral action to promote active and healthy lifestyle, including physical activity for the benefit of all people throughout their life course, and ensure a world free from malnutrition in all its forms, where all people are empowered to take responsibility for their own health supported by public regulatory measures and have access to safe drinking water and sanitation, safe, sufficient and nutritious food and enjoy diversified, balanced and healthy diets throughout their life course, with special emphasis to the nutrition needs of pregnant and lactating women, women of reproductive age and adolescent girls, and of infants and young children, especially during the first 1,000 days including, as appropriate, through exclusive breastfeeding during the first six months, with continued breastfeeding to two years of age or beyond, with appropriate complementary feeding;

29. Take measures to reduce maternal, neonatal, infant and child mortality and morbidity and increase access to quality health-care services for newborns, infants, children as well as all women before, during and after pregnancy and childbirth, including in the area of sexual and reproductive health;

30. Scale up efforts to promote healthy and active ageing, maintain and improve quality of life of older persons and to respond to the needs of the rapidly ageing population, especially the need for promotive, preventive, curative, rehabilitative and palliative care as well as specialized care and the sustainable provision of long-term care, taking into account national contexts and priorities;

31. Strengthen public health surveillance and data systems, improve routine immunization and vaccination capacities, including by providing evidence-based information on countering vaccine hesitancy, and expand vaccine coverage to prevent outbreaks as well as the spread and re-emergence of communicable and non-communicable diseases, including for vaccine-preventable diseases already eliminated as well as for ongoing eradication efforts, such as for poliomyelitis;

32. Strengthen efforts to address communicable diseases, including HIV/AIDS, tuberculosis, malaria and hepatitis as part of universal health coverage and to ensure that the fragile gains are sustained and expanded by advancing comprehensive approaches and integrated service delivery and ensuring that no one is left behind;

33. Further strengthen efforts to address non-communicable diseases, including cardiovascular diseases, cancer, chronic respiratory diseases and diabetes, as part of universal health coverage;

34. Also strengthen efforts to address eye health conditions and oral health, as well as rare diseases and neglected tropical diseases, as part of universal health coverage;

35. Scale up efforts to address the growing burden of injuries and deaths, including those related to road traffic accidents and drowning, through preventive measures as well as strengthening trauma and emergency-care systems, including essential surgery capacities as an essential part of integrated health-care delivery;

36. Implement measures to promote and improve mental health and well-being as an essential component of universal health coverage, including by scaling up comprehensive and integrated services for the prevention, including suicide prevention, as well as treatment for people with mental disorders and other mental health conditions as well as neurological disorders, providing psychosocial support, promoting well-being, strengthening the prevention and treatment of substance abuse, addressing social determinants and other health needs, and fully respecting their human rights, noting that mental disorders and other mental health conditions as well as neurological disorders are an important cause of morbidity and contribute to the non-communicable diseases burden worldwide;

37. Increase access to health services for all persons with disabilities, remove physical, attitudinal, social, structural, and financial barriers, provide quality standard of care and scale up efforts for their empowerment and inclusion, noting that persons with disabilities, representing 15% of the global population, continue to experience unmet health needs;

38. Scale up efforts to promote healthier and safer workplaces and improve access to occupational health services, noting that more than 2 million people die every year from preventable occupational diseases and injuries;

39. Pursue efficient health financing policies, including through close collaboration among relevant authorities, including finance and health authorities, to respond to unmet needs and to eliminate financial barriers to access to quality, safe, effective, affordable and essential health

services, medicines, vaccines, diagnostics and health technologies, reduce out of pocket expenditures leading to financial hardship and ensure financial risk protection for all throughout the life course, especially for the poor and those who are vulnerable or in vulnerable situations, through better allocation and use of resources, with adequate financing for primary health care, in accordance with national contexts and priorities;

40. Scale up efforts to ensure there are nationally appropriate spending targets for quality investments in public health services, consistent with national sustainable development strategies, in accordance with the Addis Ababa Action Agenda, and transition towards sustainable financing through domestic public resource mobilization;

41. Ensure sufficient domestic public spending on health, where appropriate, expand pooling of resources allocated to health, maximize efficiency and ensure equitable allocation of health spending, to deliver cost-effective, essential, affordable, timely and quality health services, improve service coverage, reduce impoverishment from health expenditure and ensure financial risk protection, while noting the role of private sector investment, as appropriate;

42. Expand quality essential health services, strengthen health systems and mobilize resources in health and other health-related Sustainable Development Goals in developing countries, noting that, according to WHO estimates, an additional 3.9 trillion USD in total by 2030 could prevent 97 million premature deaths and add between 3.1 to 8.4 years of life expectancy in low- and middle-income countries;

43. Optimize budgetary allocations on health, sufficiently broaden fiscal space, and prioritize health in public spending, with the focus on universal health coverage, while ensuring the fiscal sustainability, and in this regard encourage countries to review whether public health expenditure is adequate to ensure sufficiency and efficiency of public spending on health and, based on such review, to adequately increase public spending, as necessary, with a special emphasis on primary health care, where appropriate, in accordance with national contexts and priorities, while noting the WHO's recommended target of an additional 1% of GDP or more;

44. Promote and implement policy, legislative and regulatory measures, including fiscal measures as appropriate, aiming at minimizing the impact of the main risk factors for non-communicable diseases, and promote healthy diets and lifestyles, consistent with national policies, noting that price and tax measures can be an effective means to reduce consumption and related health-care costs and represent a potential revenue stream for financing for development in many countries;

45. Provide adequate, predictable, evidence-based and sustainable finances, while improving their effectiveness, to support national efforts in achieving universal health coverage, in accordance with national contexts and priorities, through domestic, bilateral, regional and multilateral channels, including international cooperation, financial and technical assistance, considering the use of traditional and innovative financing mechanisms such as, inter alia, the Global Fund to Fight AIDS, Tuberculosis and Malaria, GAVI, the Vaccine Alliance, the Global Financing Facility and the United Nations Trust Fund for Human Security, within their respective mandates, as well as partnerships with the private sector and other relevant stakeholders, recognizing that health financing requires global solidarity and collective effort;

46. Expand the delivery of and prioritize primary health care as a cornerstone of a sustainable people-centred, community-based and integrated health systems and the foundation for achieving universal health coverage, while strengthening effective referral system between

primary and other levels of care, recognizing that community-based services constitute a strong platform for primary health care; in public health services, consistent with national sustainable development strategies, in accordance with the Addis Ababa Action Agenda, and transition towards sustainable financing through domestic public resource mobilization;

47. Explore ways to integrate, as appropriate, safe and evidence-based traditional and complementary medicine services within national and/or subnational health systems, particularly at the level of primary health care, according to national context and priorities;

48. Scale up efforts to build and strengthen quality and people-centred health systems and enhance their performance by improving patient safety, built on a foundation of strong primary health care and coherent national policies and strategies for quality and safe health services, noting that universal health coverage can only be achieved if the services and medical products are safe and effective and are delivered in a timely, equitable, efficient, and integrated manner;

49. Promote equitable distribution of and increased access to quality, safe, effective, affordable and essential medicines, including generics, vaccines, diagnostics and health technologies to ensure affordable quality health services and their timely delivery;

50. Improve availability, affordability and efficiency of health products by increasing transparency of prices of medicines, vaccines, medical devices, diagnostics, assistive products, cell- and gene-based therapies, and other health technologies across the value chain, including through improved regulations and building constructive engagement and a stronger partnership with relevant stakeholders, including industries, private sector and civil society, in accordance with national and regional legal frameworks and contexts, to address the global concern on high prices of some health products and in this regard encourage WHO to continue its efforts to biennially convene the Fair Pricing Forum with Member States and all relevant stakeholders to discuss the affordability and transparency of prices and costs relating to health products;

51. Promote increased access to affordable, safe, effective and quality medicines, including generics, vaccines, diagnostics and health technologies, reaffirming the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) as amended, and also reaffirming the 2001 WTO Doha Declaration on the TRIPS Agreement and Public Health, which recognizes that intellectual property rights should be interpreted and implemented in a manner supportive of the right of Member States to protect public health and, in particular, to promote access to medicines for all, and notes the need for appropriate incentives in the development of new health products;

52. Explore, encourage and promote a range of innovative incentives and financing mechanisms for health research and development, including a stronger and transparent partnership between the public and the private sectors as well as the academia, recognizing the need for increasing public health-driven research and development that is needs-driven and evidence-based, guided by the core principles of safety, affordability, effectiveness, efficiency, equity and considered as a shared responsibility, as well as appropriate incentives in the development of new health products and technologies;

53. Recognize the important role played by the private sector in research and development of innovative medicines, encourage the use, where appropriate, of alternative financing mechanisms for research and development as a driver of innovation for new medicines and new uses for medicines and continue to support voluntary initiatives and incentive mechanisms that separate the cost of investment in research and development from the price and volume of

sales, facilitate equitable and affordable access to new tools and other results to be gained through research and development;

54. Engage all relevant stakeholders, including civil society, private sector and academia, as appropriate, through the establishment of participatory and transparent multi-stakeholder platforms and partnerships, to provide input to the development, implementation and evaluation of health- and social-related policies and reviewing progress for the achievement of national objectives for universal health coverage, while giving due regard to addressing and managing conflicts of interest and undue influence;

55. Strengthen the capacity of national government authorities to exercise strategic leadership and coordination role, focusing on inter-sectoral interventions, as well as strengthen the capacity of local authorities, and encourage them to engage with their respective communities and stakeholders;

56. Build effective, accountable, transparent and inclusive institutions at all levels to end corruption and ensure social justice, the rule of law, good governance and health for all;

57. Strengthen legislative and regulatory frameworks and promote policy coherence for the achievement of universal health coverage, including by enacting legislations and implementing policies that provide greater access to essential health services, products and vaccines, while also fostering awareness about the risks of substandard and falsified medical products, and assuring the quality and safety of services, products and practice of health workers as well as financial risk protection;

58. Improve regulatory capacities and further strengthen responsible and ethical regulatory and legislative system that promotes inclusiveness of all stakeholders, including public and private providers, supports innovation, guards against conflicts of interest and undue influence, responds to the evolving needs in a period of rapid technological change;

59. Provide strategic leadership on universal health coverage at the highest political level and promote greater policy coherence and coordinated actions through whole-of-government and health-in-all-policies approaches, and forge coordinated and integrated whole-of-society and multi-sectoral response, while recognizing the need to align support from all stakeholders to achieve national health goals;

60. Take immediate steps towards addressing the global shortfall of 18 million health workers in accordance with Global Strategy on Human Resources for Health: workforce 2030, and addressing the growing demand for health and social sectors which calls for the creation of 40 million health worker jobs by the year 2030, taking into account local and community health needs;

61. Develop, improve, and make available evidence-based training that is sensitive to different cultures and the specific needs of women, children and persons with disabilities, skills enhancement and education of health workers, including midwives and community health workers, as well as promote a continued education and life-long learning agenda and expand community-based health education and training in order to provide quality care for people throughout the life course;

62. Scale up efforts to promote the recruitment and retention of competent, skilled and motivated health workers, including community health workers and mental health professionals, and encourage incentives to secure the equitable distribution of qualified health workers especially in rural, hard-to-reach and underserved areas and in fields with high demands for services, including by providing decent and safe working conditions and appropriate remuneration for health workers

working in these areas, consistent with the WHO Global Code of Practice on International Recruitment of Health Personnel, noting with concern that highly trained and skilled health personnel continue to emigrate which weakens health systems in the countries of origin;

63. Provide better opportunities and working environment for women to ensure their role and leadership in the health sector, with a view to increasing the meaningful representation, engagement, participation and empowerment of all women in the workforce, addressing inequalities and eliminating biases against women, including unequal remuneration while noting that women, who currently form 70% of the health and social workforce, still often face significant barriers in taking leadership and decision making roles;

64. Take necessary steps at the country level to protect health workers from all forms of violence, attacks, harassment and discriminatory practices, and to promote their decent and safe working environment and conditions at all times as well as ensure health workers' physical and mental health by promoting policies conducive to healthy lifestyles;

65. Strengthen capacity on health intervention and technology assessment, data collection and analysis, while respecting patient privacy and promoting data protection, to achieve evidence-based decisions at all levels, acknowledging the role of digital health tools in empowering patients, giving them access to their own healthcare information, promoting health literacy, and strengthening patient involvement in clinical decision-making with a focus on health professional-patient communication;

66. Invest in and encourage ethical and public-health-driven use of relevant evidence-based and user-friendly technologies, including digital technologies, and innovation to increase access to quality health and related social services and relevant information, improve the cost-effectiveness of health systems and efficiency in the provision and delivery of quality care in a manner that recognizes the need to build and strengthen interoperable and integrated health information systems for the management of health systems and public health surveillance, as well as the need to protect data and privacy and narrow the digital divide;

67. Strengthen health information systems and collect quality, timely and reliable data, including vital statistics, disaggregated by income, sex, age, race, ethnicity, migratory status, disability, geographic location, and other characteristics relevant in national contexts as required to monitor progress and identify gaps in the universal and inclusive achievement of SDG3 and all other health-related Sustainable Development Goals, while protecting the privacy of data that could be linked to individuals, and to ensure that the statistics used in the monitoring progress can capture the actual progress made on the ground, for the achievement of universal health coverage, in line with the 2030 Agenda;

68. Ensure, by 2030, universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes, which is fundamental to the achievement of universal health coverage, while reaffirming the commitments to ensure universal access to sexual and reproductive health and reproductive rights in accordance with the Programme of Action of the International Conference on Population and Development and the Beijing Platform for Action and the outcome documents of their review conferences;

69. Mainstream a gender perspective on a systems-wide basis when designing, implementing and monitoring health policies, taking into account the specific needs of all women and girls, with a view to achieving gender equality and the empowerment of women in health policies and health systems delivery and the realization of their human rights, consistent with national

legislations and in conformity with universally recognized international human rights, acknowledging that the human rights of women include their right to have control over and decide freely and responsibly on all matters related to their sexuality, including sexual and reproductive health, free of coercion, discrimination and violence;

70. Ensure that no one is left behind, with an endeavour to reach the furthest behind first, founded on the dignity of the human person and reflecting the principles of equality and non-discrimination, as well as to empower those who are vulnerable or in vulnerable situations and address their physical and mental health needs which are reflected in the 2030 Agenda for Sustainable Development, including all children, youth, persons with disabilities, people living with HIV/AIDS, older persons, indigenous peoples, refugees and internally displaced persons and migrants;

71. Address the particular needs and vulnerabilities of migrants, refugees, internally displaced persons and indigenous peoples which may include assistance, health care, psychological and other counselling services, in accordance with relevant international commitments, and in line with national contexts and priorities;

72. Promote strong and resilient health systems, reaching those who are vulnerable or in vulnerable situations, and capable of effectively implementing the International Health Regulations (2005), ensuring pandemic preparedness and the prevention and detection of and response to any outbreak;

73. Promote more coherent and inclusive approaches to safeguard universal health coverage in emergencies, including through international cooperation, ensuring the continuum and provision of essential health services and public health functions, in line with humanitarian principles;

74. Enhance emergency health preparedness and response systems, as well as strengthen capacities at national, regional and international levels, including to mitigate the impacts of climate change and natural disasters on health;

75. In accordance with international humanitarian law, respect and protect, in situations of armed conflict, medical personnel and humanitarian personnel exclusively engaged in medical duties, their means of transport and equipment, and hospitals and other medical facilities, which must not be unlawfully attacked, and ensure that the wounded and sick receive, to the fullest extent practicable and with the least possible delay, the medical care and attention required;

76. Enhance cooperation at the national, regional and global levels to address antimicrobial resistance, using an integrated and systems-based one-health approach, including through health system strengthening, capacity-building, including for research and regulatory capacity, and technical support and ensure equitable access to affordable, safe, effective and quality existing and new antimicrobial medicines, vaccines, and diagnostics as well as effective stewardship, as antimicrobial resistance poses a challenge to achieving UHC, noting the work of the Inter-Agency Coordination Group on AMR and its recommendations as contained in the Secretary-General's report on AMR (A/73/869) and look forward to the discussion thereof during the 74th session of the General Assembly, taking into account World Health Assembly resolution WHA72.5;

77. Revitalize and promote strong global partnerships with all relevant stakeholders to collaboratively support the efforts of Member States, as appropriate, to achieve universal health coverage and other health-related targets of the Sustainable Development Goals, including

through technical support, capacity building and strengthening advocacy, building on existing global networks such as the International Health Partnership for UHC2030, and in this regard take note of the upcoming presentation of the global action plan for healthy lives and well-being for all;

78. Increase global awareness, international solidarity, international cooperation and action towards the achievement of universal health coverage by promoting national, regional and global collaborative frameworks and fora, including through the commemoration of International Universal health coverage Day on 12 December of every year;

79. Set measurable national targets and strengthen national monitoring and evaluation platforms, as appropriate, in line with the 2030 Agenda for Sustainable Development, to support regular tracking of the progress made for the achievement of universal health coverage by 2030;

80. Leverage the full potential of the multilateral system, in collaboration with Member States upon their request, and call upon the relevant entities of the United Nations development system, within their respective mandates, primarily WHO as the leading agency on health, as well as the reinvigorated UN Resident Coordinators and the UN Country Teams, within their respective mandates, as well as other relevant global development and health actors, including civil society, private sector and academia, to assist and support countries in their efforts to achieve universal health coverage at the national level, in accordance with their respective national contexts, priorities and competences;

81. Request the Secretary-General to continue engaging with Member States to sustain and further strengthen the political momentum on universal health coverage and, in close collaboration with relevant UN agencies and other stakeholders including regional organizations, to strengthen existing initiatives that are led and coordinated by the WHO to provide assistance to Member States, upon their request, towards the achievement of universal health coverage and all health-related targets of the Sustainable Development Goals;

As a follow-up to this political declaration, we:

82. Request the Secretary-General to provide, in consultation with the WHO and other relevant agencies, a progress report during the seventy-fifth session of the General Assembly, and a report including recommendations on the implementation of the present declaration towards achieving universal health coverage during the seventy-seventh session of the General Assembly, which will serve to inform the high-level meeting to be convened in 2023;

83. Decide to convene a high-level meeting on UHC in 2023 in New York, aimed to undertake a comprehensive review on the implementation of the present declaration to identify gaps and solutions to accelerate progress towards the achievement of universal health coverage by 2030, the scope and modalities of which shall be decided no later than the seventy-fifth session of the General Assembly, taking into consideration the outcomes of other existing health-related processes and the revitalization of the work of the General Assembly.

