A compilation of technical papers presented during Regional Meeting, Bangkok, Thailand.
16-18 December, 2014.
Section I Literature Review for GSPA

Section II Technical Papers
Section I

Literature Review for GSPA

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Acronym

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<th>WHO Advisory Committee on Health Research</th>
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<td>African Council for Sustainable Health Development</td>
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<td>AHHRF</td>
<td>African Health Research Forum</td>
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<td>AFRO</td>
<td>WHO African Regional Office</td>
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<td>aHIF</td>
<td>Antibiotic Health Impact Fund</td>
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<td>ALIFAR</td>
<td>Asociacion Latinoamericana de Industrias Farmaceuticas</td>
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<td>AMC</td>
<td>Advanced Market Commitment</td>
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<td>AMREF</td>
<td>African Medical and Research Foundation</td>
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<td>ANDi</td>
<td>African Network for Drugs and Diagnostics Innovation</td>
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<td>APAST</td>
<td>ASEAN Plan of Action on Science and Technology</td>
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<td>API</td>
<td>Active Pharmaceutical Ingredients</td>
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<td>ASEAN</td>
<td>Association of South East Asian Nations</td>
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<td>ASEAN-NDI</td>
<td>ASEAN Network for Drugs, Diagnostics, Vaccines, and Traditional Medicines Innovation</td>
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<td>BARDA</td>
<td>Biomedical Advanced Research and Development Authority</td>
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<td>BRICS</td>
<td>Brazil, Russia, India, China and South Africa</td>
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<tr>
<td>CAM</td>
<td>Complementary and Alternative Medicine</td>
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<td>CARICOM</td>
<td>Caribbean Community</td>
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<td>CIHR</td>
<td>Canadian Institute of Health Research</td>
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<td>CIPIH</td>
<td>Commission in Intellectual Property Rights, Innovation and Public Health</td>
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<td>COHRED</td>
<td>Council on Health Research and Development</td>
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<td>CoP</td>
<td>Community of Practice</td>
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<td>CSIR</td>
<td>Council of Scientific and Industrial Research (India)</td>
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<td>DEC</td>
<td>Disease Endemic Country</td>
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<td>DNDI</td>
<td>Drugs for Neglected Diseases Initiative</td>
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<td>DPCO</td>
<td>Drug Price Control Order</td>
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<td>DTL</td>
<td>Drug Testing Laboratory</td>
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<td>EDCTP</td>
<td>European and Developing Countries Clinical Trials Partnership</td>
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<td>EMRO</td>
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<td>EQUINET</td>
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<td>EURO</td>
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<td>EWG</td>
<td>Expert Working Group on Research and Development : Financing and Coordination</td>
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<td>FIFARMA</td>
<td>Federacion Latinoamericana de la Industria Farmaceutica</td>
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<td>GHO</td>
<td>Global Health Observatory</td>
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<td>GPO</td>
<td>Government Pharmaceutical Organization</td>
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<td>GSK</td>
<td>GlaxoSmithKline</td>
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<td>GSPA-PHI</td>
<td>Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property</td>
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<td>HINARI</td>
<td>Health Inter Network Access to Research Initiative</td>
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<td>HMN</td>
<td>Health Metrics Network</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>HR-HR</td>
<td>Human Resources for Health Research</td>
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<td>HHS</td>
<td>US Dept. of Health and Human Services</td>
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<td>ICMR</td>
<td>Indian Council of Medical Research</td>
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<td>ICTRP</td>
<td>WHO International Clinical Trials Registry Platform</td>
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<td>IDRC</td>
<td>International Development Research Centre</td>
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<td>IFC</td>
<td>International Finance Corporation</td>
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<td>IGWG</td>
<td>Inter-governmental Working Group on Public Health, Innovation and Intellectual Property</td>
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<td>IVI</td>
<td>International Vaccine Institute</td>
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<td>LAIV</td>
<td>Live Attenuated Influenza Vaccine</td>
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<td>Lao PDR</td>
<td>Lao People’s Democratic Republic</td>
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<td>MERCOSUR</td>
<td>Mercado Comun del Sur</td>
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<td>NAFTA</td>
<td>North American Free Trade Agreement</td>
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<td>NCD</td>
<td>Non-communicable Diseases</td>
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<td>NCL</td>
<td>National Control laboratory</td>
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<td>ND4BB</td>
<td>New Drugs for Bad Bugs Program</td>
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<td>NEPAD</td>
<td>New Partnerships for Africa’s Development</td>
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<td>NHRS</td>
<td>National Health Research System</td>
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<td>NIH</td>
<td>US National Institutes of Health</td>
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<td>NSTDA</td>
<td>National Science and Technology Development Agency of Thailand</td>
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<td>NRA</td>
<td>National Regulatory Authority</td>
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<td>NRCT</td>
<td>National Research Council of Thailand</td>
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<td>NVI</td>
<td>Netherlands Vaccine Institute</td>
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<td>OSDDI</td>
<td>Open Source Drug Discovery Infrastructure</td>
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<td>PAHO</td>
<td>Pan American Health Organization</td>
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<td>PANDRH</td>
<td>Pan American Network for Drug Regulatory Harmonization</td>
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<td>PATH</td>
<td>Program for Appropriate Technologies in Health</td>
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<td>PDP</td>
<td>Product Development Partnership</td>
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<tr>
<td>PLAIV</td>
<td>Pandemic Live Attenuated Influenza Vaccine</td>
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<td>PPP</td>
<td>Public Private Partnership</td>
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<td>SEAICRN</td>
<td>South East Asia Infectious Disease Clinical Research Network</td>
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<td>SEAR</td>
<td>South East Asian Region</td>
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<td>SEARO</td>
<td>South East Asia Regional Office of WHO</td>
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<td>SGC</td>
<td>Structural Genomics Consortium</td>
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<td>SICA</td>
<td>Sistema de la Integracion Centroamericana</td>
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<td>SII</td>
<td>Serum Institute of India</td>
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<td>T&amp;CM</td>
<td>Tropical and Complementary Medicine</td>
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<td>TDR</td>
<td>Special Programme for Research and Training on Tropical Diseases</td>
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<td>TRF</td>
<td>Thailand Research Fund</td>
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<td>TropIKA.net</td>
<td>Tropical Disease Research to Foster Innovation and Knowledge Application</td>
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<td>TMK</td>
<td>Traditional Medicine Knowledge</td>
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<td>TRIPS</td>
<td>Agreement on Trade-related Aspects of Intellectual Property Rights</td>
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<td>UNCTAD</td>
<td>United Nations Commission on Trade and Development</td>
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<td>UNDP</td>
<td>United Nations Development Program</td>
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<td>UNESCOAP</td>
<td>United Nations Economic and Social Commission for Asia and the Pacific</td>
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Executive Summary

The WHA62.16 resolution on Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property has asked “to conduct an overall programme review of the GSPA-PHI in 2014 on its achievement, remaining challenges and recommendations on the way forward and report to the Assembly in 2015 through the Executive Board.”

The WHA resolution 61.21 identified a number of deliverables under GSPA-PHI and aims to promote new thinking on innovation, transfer of technology and access to medicines.

A literature search on the 25 sub-elements and 8 main elements of GSPA, with the findings analyzed and delineated based on regional and global situation has been done by SEAMEO - TROPMED on the request of WHO/SEARO

Included in the search were literature which were published or which referred to activities which were implemented from 2008 onwards. These include journal articles relevant to any of the 8 elements and 25 sub-elements of the GSPA-PHI; reports of meetings held at the global, regional and national levels on areas which are either related solely to the GSPA-PHI, or where GSPA-PHI and/or related issues are items in the agenda; uploaded files of presentations made during these meetings; and reports of commissioned studies related to various aspects of GSPA-PHI.

The results indicate that of the 8 GSPA-PHI elements, it is in the area of prioritizing research and development needs (element #1) where much progress has been done, especially at the global level. At the regional and national levels, the areas where much work still needs to be done are in the application and management of intellectual property to contribute to innovation and promote public health (element #5); improving delivery and access (element #6); promoting sustainable financing mechanisms (element #7); and establishing monitoring and reporting systems (element #8).

Recommendations

Recommendations given, in terms of future action to be implemented, are:

- In the area of local production of medicines, a primary objective must be the identification of therapeutic areas and regions for which existing production does not meet local needs, including needs for long-term sustainable supply. Objectives of the work programme/action plans to be developed should be formulated to address those unmet needs.

- Expansion of International partnerships that provide technical assistance and access to technology;

- Engagement of research organizations with country leadership and other stakeholders to assess the adequacy of current national research capacity and use the assessment results as inputs in...
determining the most effective role they can play to support the development of research capacity that addresses the health and development needs of the country;

- Expansion of opportunities for production staff of local drug manufacturers to include practical training which would complement the theoretical training provided by academic institutions. Such type of training is amenable to both north-south and south-south cooperation, since several developing countries are no home to advanced industries that could provide training opportunities to nationals of developing countries.

- Capacity building on how to negotiate effective technology transfer agreements may be useful, particularly for firms with limited experience in this area.

- Ongoing efforts in training national drug regulatory authorities and policy makers on how to implement TRIPS in a manner that protects public health and expands the space for local production should be strongly supported and continued.

- Countries need to streamline their system for regulating pharmaceutical and biotechnology R&D needs, and strengthen their systems and capacity for evaluating new technologies. At the same time, international systems for assessing and recommending products, especially WHO’s prequalification program for diagnostics need to be expanded so they can handle more products more rapidly.

- WHO should continue to work with national and regional regulatory authorities to coordinate and further integrate rules and mechanisms for approving and monitoring operation of pharmaceutical production facilities.

- Both the government of Member States and international donors should expand financing for promising neglected disease product development projects, including for late-stage clinical trials and for new innovation-driven firms.

- There is a need for improved information about ongoing initiatives to provide a stronger evidence base for policy analysis and recommendations. A methodical, comprehensive, regularly updated and publicly accessible database of relevant initiatives is currently lacking but is badly needed in the current fragmented landscape.

- Start activities for the development of the Regional Health Observatory in a phased way in 3 steps, as recommended by the 2012 Report to the Secretariat, as follows: 1) research phase; 2) planning phase; and 3) pilot-testing phase. The Region should already start the research phase (needs assessment and situational analysis) for this undertaking.

- There is a need to make the current GSPA-PHI assessment tool more user friendly in order to encourage more countries to use it. Sri Lanka’s experience can be a useful benchmark.
1. Background

In May 2003, a landmark document, *WHA56.27 (Intellectual Property Rights, Innovation and Public Health)* was adopted by the 56th World Health Assembly of the World Health Organization.¹ This marked the start of the systematic, organized and coordinated conduct of global initiatives to analyse intellectual property rights, innovation and public health, as well as to provide adequate funding, incentive mechanisms and promote research and development for the development of new products and technologies against diseases that disproportionately affect developing countries. This was the basis for the establishment of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) in 2004 which made an in-depth analysis of the issues, and presented 60 recommendations in its report which was published in 2006.²

From 2003 onwards, the World Health Assembly adopted several resolutions, established several bodies and conducted a number of meetings to fine-tune the original recommendations of the CIPIH report. A listing of such resolutions, working groups and meetings is presented in Annex 1, with their corresponding recommendations.

At the regional and national levels, a significant milestone was the adoption by the World Health Assembly of Resolution WHA65.22 in 2012, which urged Member States to hold national-level consultations to discuss the CEWG Report, and analyse the feasibility of its recommendations during Regional Committee Meetings and in regional and national consultations.⁹ SEAR has been an active leader in this area. In particular, the 65th SEA Regional Committee Meeting, Yogyakarta, Indonesia, Sept. 2012 adopted Regional Resolution SEA/RC65/R3 (Consultative Expert Working Group on Research and Development: Financing and Coordination) which was later used as the working draft and the major input for the draft resolution adopted at the Open-ended meeting of Member States on the follow-up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination in Geneva on 26-28 November 2012.¹²,¹⁰ This meeting was chaired by Dr. Viroj Tangcharoensathien, Thailand.

Since 2012, several activities have been conducted in the region in relation to the CEWG recommendations. An important follow-up activity to the adoption of South East Asia Regional Committee resolution, SEA/RC65/R3. Regional meetings and consultations were conducted to facilitate the development of action plans. A listing of the regional activities undertaken related to CEWG recommendations are presented in Annex 2.

1.1 Terms of Reference

SEAMEO - TROPMED Thailand, which has earlier been involved in developing documents for the Consultative Expert Working Group under Element 7 of GSPA, was asked by WHO/SEARO to undertake a project with the following terms of reference:

- Perform literature search on the 25 sub-elements and 8 main elements of GSPA;
- Analyze and delineate the findings based on regional and global situation;
- Identify a draft set of suggested next steps for each of the 25 sub-elements for discussion; and
Based on the findings of the literature search and gaps identified, come up with a survey questionnaire tool that can be used at the Regional Consultation Meeting to complete the picture of regional situational analysis.

This document presents the results of the literature review.
2. Methodology

2.1 Coverage of Literature Review

The literature reviewed includes:

a. Journal articles relevant to any of the 8 elements and 25 sub-elements of the GSPA-PHI;

b. Reports of meetings held at the global, regional and national levels on areas which are either related solely to the GSPA-PHI, or where GSPA-PHI. Uploaded files of presentations made during these meetings; and

c. Reports of commissioned studies related to various aspects of GSPA-PHI

Since the GSPA-PHI is a WHA Resolution, the first step taken in searching for the above documents was to access the websites of the following:

a. WHO/HQ as well as those of the regional offices..

b. Special programmes/projects/initiatives based in WHO which are related to GSPA-PHI like TDR, COHRED, IVR and HINARI,

c. Non-WHO-based programmes, initiatives, organizations, networks involved in activities related to GSPA-PHI like PATH, BRICS, DNDi, ASEAN-NDI, etc.

Additional literature not posted in the above mentioned websites were searched using the following search engines:


b. PLOS Medicine – An open access weekly journal for peer-reviewed literature; and

c. Google Scholar – Searches articles from a wide variety of academic publishers, professional societies, preprint repositories and universities.,

Included in the search were literatures which were published or which referred to activities which were implemented from 2008 onwards. Exceptions were materials which serve as the foundation of succeeding activities like the documentation of the COHRED assessment tools for national health research systems which were developed earlier than 2008. A documentation of a conference on Human Resources for Health Research held in Africa in 2006 was also included since this was the only conference conducted covering this topic.

All materials retrieved were first sorted according to the 8 elements of the GSPA-PHI, and then further according to the 25 sub-elements. Within each sub-element, a third layer of categorization was applied according to geographic area of coverage of the initiative or activity (regional or global).
For purposes of this paper, the following definitions were used:

a. **Regional** – this category was considered as synonymous to the South East Asian Region (SEAR), as defined by WHO. It refers to any activity conducted at the regional level within SEAR, or involving any of the 11 member states of the region. Hence, under this definition, activities of ASEAN related to GSPA-PHI are considered as regional since 3 of the ASEAN-member countries (Indonesia, Thailand and Myanmar) are SEAR Member States.

b. **Global** – this category was considered as synonymous to non-SEAR. It refers to any activity conducted in regions other than SEAR, or involving a country which is not a SEAR member state. It includes activities at the global, regional and national levels.

As expected, not sufficient documents were found as a result it was deemed necessary to supplement the literature review with a survey questionnaire, completed by Member States and research institutions, to a get a true sense of the status of various elements of GSPA-PHI. The results of this survey are presented in another report.

### 2.2 Limitations

The project covered an extremely wide scope -- 25 sub-elements classified into regional and global, or 50 sub-topics altogether. It was difficult to do a complete and comprehensive review of documents for about 50 sub-topics within the 6 months allotted for the project.

A very evident overlapping was seen with respect of both the sub-elements as well as the literature covered. This overlapping may have led to either omission or an over representation of facts.

At the regional level, there is bias towards the bigger countries, specifically India and Thailand, because these are the countries which are good in documenting and disseminating their activities. Hence most of the literature retrieved at the regional level referred to these countries. This bias is counteracted by including the activities identified in the country reports presented during the Regional Meeting for Assessment of Progress in Implementing the GSPA-PHI held in Bangkok on December 16-18, 2014.
3. CURRENT STATUS OF GSPA ELEMENTS: REGIONAL AND GLOBAL LEVELS

1. PRIORITIZING RESEARCH AND DEVELOPMENT NEEDS

1.1 Mapping global research and development

The main objective of the first sub-element under prioritizing research and development needs is to identify gaps in R&D on diseases that disproportionately affect developing countries. Mapping is important in order to coordinate and align investments in health R&D with global public health priorities.

The first systematic and comprehensive mapping of health R&D at the global level was undertaken by COHRED in 2005. The mapping activity helps identify areas which need strengthening, and help policy makers to decide investment target areas in order to improve the performance and achievement of targets of national health research. Since 2005, COHRED has mapped the national health research systems of about 80 countries.

The mapping of R&D for infectious diseases of poverty is part of the strategy and business plan of the Special Programme for Research and Training in Tropical Diseases (TDR) for the year 2008-2013. Under this Plan, the first 3 specific objectives of its Business Line 1 which is on stewardship are to:

1. provide a global information platform on health research needs, opportunities and activities on infectious diseases of poverty;

2. develop an evidence and analysis-driven forum for the identification of priority needs and major research gaps through stakeholder consultations and to enhance the relevance of infectious disease research priorities to control needs; and

3. provide a neutral platform for partners to discuss their activities, reach the highest possible level of consensus and enhance their collective efficiency and advocacy for infectious diseases of the poor with active involvement of diseases endemic countries.

To meet these specific objectives, the expected end-products include, among others, the following:

- an online knowledge platform for infectious diseases research with equitable access to comprehensive information on research needs, activities and achievements; highlights of scientific publications; access to published articles; news and review articles on critical issues, discussion forums, resources, multimedia. For example TropIKA.net (Tropical Diseases Research to Foster Innovation and Knowledge Application), online knowledge platform
Up-to-date published reports on research opportunities, needs and priorities, and research achievements for individual infectious diseases or cross-disease issues that are widely accepted and promote disease endemic country (DEC) research;

Comprehensive analyses of regional or global research needs, science opportunities and challenges in health systems that stimulate high level fora and action; and

Biennial report on infectious diseases research; priority research needs, gaps and global progress like the Global Report for Research on Infectious Diseases of Poverty published in 2012 by TDR.

One of the major challenges in mapping health R&D is the data source. A number of researchers have explored different data collection sources and methodologies for purposes of mapping. Viergiver, et al, identified gaps in health research and development by using data from the WHO International Clinical Trials Registry Platform (ICTRP). On the other hand, Røttingen et al used international databases to provide a comprehensive description of available data sources, propose a set of indicators for monitoring the global landscape for health research and development, and present a sample of country indicators on research inputs (investments), processes (clinical trials) and outputs (publications). Their paper confirmed that substantial gaps in the global landscape for health R&D still exist, with too few investments being targeted towards the health needs of low and middle-income countries. Their results showed the need for better data to improve priority setting and coordination for health R&D, in order to ensure that resources are allocated to diseases and regions where they are most needed.

Regional

Mapping of health R&D among the ASEAN-member countries was conducted from November 2009 to December 2010, as part of the groundwork for the establishment of the ASEAN Network for Drugs, Diagnostics, Vaccines, and Traditional Medicines Innovation (ASEAN-NDI). Data for the mapping exercise was collected via surveys and key informant interviews among researchers and research institutions. A review of Elsevier’s Scopus database was also done. It was carried-out in order to assess the product R&D landscape for the triple burden (infectious tropical, non-communicable and preventable diseases) of disease in the region. Specifically, it aimed to:

a. map-out the capabilities of the ASEAN member countries on drugs, diagnostics, vaccines and traditional medicine innovation on infectious tropical diseases;

b. create a database of institutions, networks and initiatives with capacities for innovation; and

c. provide the template for the establishment of an ASEAN regional network for innovation in product research and development.

The results of the mapping exercise showed a wide and diverse R&D capacity among ASEAN countries on drugs, diagnostics, vaccines and traditional medicine. For example, the number of bio-medical articles published by countries between 2005 and 2009 ranged from 86 in Vietnam to
12,568 in Thailand. While all ASEAN member countries reported as being involved in drug development, the number of institutions involved in this activity ranged from 3 in Lao PDR to 90 in Thailand.  

A more recent mapping with focus on research capacity was done in 2011 in connection with a WHO-SEARO project on mapping centers of expertise on tropical diseases in the region. The objectives of this activity were to define tropical disease and to map institutions that could become centers of excellence for networking with other institutions to bridge the gap for qualitative research and delivery of quality medical intervention techniques, training and procedures for the constituent members. It was conducted in 7 countries (Bangladesh, India, Indonesia, Myanmar, Nepal and Thailand), and the results were presented during the Regional Meeting of Centers of Expertise on Tropical Medicine which was held in Faridabad, India on 28-30 November 2011. Individual reports on the results on the detailed results for each country are also available.

Global

Among the first regions where the COHRED mapping of national health research systems was conducted was in the Eastern Mediterranean region. The mapping covered ten countries namely Bahrain, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Tunisia, United Arab Emirates and Yemen. Planning for the project started in late 2005, and the report was published in 2008. The mapping included people, structures, institutions and policies that make-up the national health research system (NHRS) and covered the following areas:

a. governance and management of NHRS
b. institutions engaged in ‘research for health’
c. key stakeholders involved in ‘research for health’
d. available literature and data review on ‘research for health’.

The results showed that only a few of the countries have a formal NHRS, and most lack the essential building blocks for an effective system. Only one out of the 10 participating countries established a M&E system for its NHRS and not a single country reported having systematic efforts to feed research results into decision-making within the health sector.

In 2012, the European and Developing Countries Clinical Trials Partnership (EDCTP) commissioned a study to conduct a landscape analysis of health research and national funding commitments for poverty-related and neglected infectious diseases in sub-Saharan Africa. The objective of this study was to review the current state of health research, the funding landscape, and research capacity in the field of HIV/AIDS, TB, malaria, neglected infectious disease, and health systems/operational research in sub-Saharan Africa. Data sources were semi-structured questionnaires and the conduct of in-depth interviews with key stakeholders in sub-Saharan African governments, research institutions and international organizations. Among the questions asked in the survey were to identify four barriers to the development of clinical research in their country. The most common response given was lack of funding (40%), followed closely by the lack of understanding on the part of the policy makers of the importance and benefits of research.
The two other most commonly cited factors were lack of human resources and lack of infrastructure.

1.2 Formulating explicit prioritized strategies for research and development

A draft working paper prepared by the WHO Secretariat on coordination and priority setting in R&D to meet health needs in developing countries identified five distinct but complementary areas of work which can contribute to improved coordination and prioritization of R&D. These are:

- improved information sharing;
- establishing new fora to discuss health R&D;
- putting in place a global advisory body by adopting existing structures (e.g., WHO Advisory Committee on Health Research (ACHR), etc.);
- using demonstration projects to explore new modes of coordination; and
- developing new standards and norms to improve priority setting methodology, to report priorities, and to compare priorities across disease areas.

The establishment of the Global Observatory is expected to improve information sharing and function as a library.

Regional

A regional consultation for developing a strategic work plan as a follow-up of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) was held in Bangkok by SEARO on 25-26 July 2013. During the meeting, the development of norms and standards for classification of health R&D towards setting-up of R&D observatories were discussed, and a template for a proposed classification grid was presented for pilot-testing. The consultation also identified seven priority areas based on the public health needs of Member States of the Region and for which demonstration projects can be implemented to deliver health products.

The following recommendations were agreed on during the consultation in relation to the development of norms and standards for classification of health R&D towards setting-up of R&D observatories:

- A national R&D laboratory may be set-up to collect, analyze, coordinate, prioritize and monitor R&D resource flows from the public and private sectors. Member states may develop modalities and identify institutional entities to develop, establish, maintain and manage health R&D observatories.

- The scope of the observatory may include data on R&D infrastructure, human resources and financial flows, intellectual property and project related to technology transfer.

- Member States may pilot test the proposed classification grid for norms and standards for R&D in terms of diseases, product development and policy. Member States which
have collected data for purposes of the consultation may revisit it to test the proposed classification system and suggest improvements, if any.

d. A technical/national meeting/review may be organized to validate these outcomes before these are recommended for consideration by WHO. The consultation also identified and ranked seven potential priority areas for R&D demonstration projects and proposed a scheme for informal collaboration by identifying lead and participating countries among the Member States for each project. This is shown in Table 1 below.

Table 1. Proposed informal collaboration for demonstration projects among SEAR Member States

<table>
<thead>
<tr>
<th>Rank</th>
<th>Priority Areas</th>
<th>Lead Country</th>
<th>Participating Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Combating tuberculosis in the Region (development of diagnostics, vaccines, and new anti-TB drugs)</td>
<td>India</td>
<td>Indonesia, Timor-Leste</td>
</tr>
<tr>
<td>2</td>
<td>Combating global diabetes by development of new diagnostics and new anti-diabetes drugs (both traditional and modern medicines)</td>
<td>Sri Lanka</td>
<td>Bangladesh, Thailand</td>
</tr>
<tr>
<td>3</td>
<td>New point-of-care diagnostics for fever of unknown origin in field settings</td>
<td>India</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>R&amp;D in new drugs and diagnostics for cancer (type of cancer to be identified referring to disease burden)</td>
<td>Indonesia</td>
<td>Bangladesh, Thailand</td>
</tr>
<tr>
<td>5</td>
<td>Dengue vaccine</td>
<td>Thailand</td>
<td>India, Maldives</td>
</tr>
<tr>
<td>6</td>
<td>Pan-serotype pneumococcal vaccine</td>
<td>India</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Development of active pharmaceutical ingredients for medicines</td>
<td>Bangladesh</td>
<td></td>
</tr>
</tbody>
</table>


At the national level, SEAR Member States have conducted activities to prioritize areas for health R&D. Such activities were included as part of their report during the meeting held in Bangkok in December 2014 to assess progress in implementing the 8 elements and 25 sub-elements of GSPA-PHI in SEAR. The results of the prioritization activities reported by the countries are presented in Annex3.

Global

In 2008-2009, the New Partnerships for Africa’s Development (NEPAD) and COHRED conducted a study on the pharmaceutical innovation landscape and current approaches in Africa. The results for this study provided the evidence-base for the development of the initiative called Strengthening...
Pharmaceutical Innovation in Africa which is a partnership between the African Union, NEPAD and COHRED. Part of this initiative is the development of the Pharmaceutical Innovation Framework and Grid tools which were designed to help countries to move forward in putting mechanisms for GSPA-PHI implementation into action at the national level. The tool helps countries do self-assessments, develop strategies, build capacity and partnerships to engage in innovation and improve access to essential medicines.  

In 2011, the African Health Observatory, an information technology platform designed to facilitate multi-stakeholder collaboration and partnership in accessing and using information for strengthening national health systems and improving health outcomes, became operational, with the main objective of serving as a tool in addressing priority health problems in the Region, and bringing together key regional and global stakeholders for this purpose. It is the repository of the best health information available, and serves as tool to monitor health status and trends, and is expected to interact with national health observatories in the Member States to contribute to M&E, data collection, and analysis at the national level.

In the area of demonstration projects, the Secretariat, on 7 – 10 May 2014, convened four meetings with stakeholders interested in funding and or implementing the 4 projects shortlisted during the Global Technical Consultative Meeting of Experts held on 3-4 December 2013. These projects are:

a) The Visceral Leishmaniasis (VL) Global R&D and Access Initiative (Proponent: Drugs for Neglected Diseases Initiative)

b) Development of Class D CpG oligodeoxynucleotides (D35) as an adjunct to chemotherapy for cutaneous leishmaniasis and post kala-azar dermal leishmaniasis (Proponents: United States Food and Drug Administration; Osaka University, et al.)

c) Exploiting the pathogen box : an international open-source collaboration to accelerate drug development in addressing diseases of poverty (Proponent: Medicines for Malaria Venture)

d) Development of easy-to-use and affordable biomarkers as diagnosis for types II and III diseases (Proponents: African Network for Drugs and Diagnostics Innovation, Chinese Network for Drugs and Diagnostics Innovation, et al)

The assessment framework and indicators to measure success of the R&D demonstration projects were earlier developed in an earlier meeting convened in Geneva on 10 March 2014 to examine additional information received on the 7+1 demonstration projects originally short-listed.

1.3 Encouraging research and development in traditional medicine

On 8 November 2008, the WHO Congress on Traditional Medicine held in Beijing, China, adopted the Beijing Declaration on Traditional Medicine which promoted the safe and effective use of traditional medicine, and called on WHO Member States and other stakeholders to take steps to integrate traditional medicine into national health systems. In this Declaration, the development
of traditional medicine based on research and innovation in line with the GSPA-PHI was explicitly indicated as one of the six articles, namely:

1. Knowledge of traditional medicine, treatments and practices should be respected, preserved, promoted and communicated widely and appropriately based on the circumstances in each country.

2. Governments have a responsibility for the health of their people and should formulate national policies, regulations and standards, as part of comprehensive national health systems to ensure appropriate, safe and effective use of traditional medicine.

3. Recognizing the progress of many governments to date in integrating traditional medicine into their national health systems, those who have not yet done so are called to take action.

4. Traditional medicine should be further developed based on research and innovation in line with the "Global strategy and plan of action on public health, innovation and intellectual property" adopted at the Sixty-first World Health Assembly in resolution WHA61.21 in 2008. Governments, international organizations and other stakeholders should collaborate in implementing GSPA-PHI.

5. Governments should establish systems for the qualification, accreditation or licensing of traditional medicine practitioners. Traditional medicine practitioners should upgrade their knowledge and skills based on national requirements.

6. The communication between conventional and traditional medicine providers should be strengthened and appropriate training programmes be established for health professionals, medical students and relevant researchers.

During the Sixty-Second World Health Assembly held on May 2009, the resolution on traditional medicine (WHA62.13) was presented which urged the adoption and implementation of the Beijing Declaration on Traditional Medicine by Member States in accordance with their capacities, priorities, relevant legislation and circumstances. In the same document, the Director General was requested to give due consideration to specific actions related to traditional medicine in the implementation of the GSPA-PHI. Among the strategic actions recommended for Member States are to:

a. Promote R&D, innovation and knowledge management;

b. Encourage knowledge generation, translation and dissemination by establishing a comprehensive and inclusive approach to R&D on traditional and complementary medicine (T&CM) including quality and cost effectiveness; and

c. Developing a research agenda on T&CM which acknowledges and includes various types of research models where appropriate.
In the same document, the following strategic actions are recommended for partners and stakeholders, among others:

a. Develop research methodologies consistent with T&CM theories and practice;

b. Build up the capacity and capability for international research, including such issues as the adequate protection of intellectual property and the prevention of possible misappropriation; and

c. Support international research collaboration on T&CM

Regional

An important development in the area of traditional medicine in the Region was the launching of the ASEAN-NDI in 2011, which has, as one of its goals, the establishment and development of an ASEAN-wide research collaboration on traditional medicine. In line with this goal, the first Community of Practice (CoP) Meeting on Traditional Medicine was held in the Philippines in June 2014 to discuss country status and initiatives on traditional medicine and identify possible areas of collaboration. Specific areas of discussion were the expectations and challenges in relation to activities identified in the ASEAN-NDI Strategic and Business Plan. These include the development of an ASEAN-wide R&D project on traditional medicine; collaboration with researchers from ASEAN-member countries; initiation of external funding request; and M&E of research implementation and outcomes.

On 12-14 February 2013, the International Conference on Traditional Medicine for South East Asian Countries was held in New Delhi. The conference concluded with the adoption of the Delhi Declaration on Traditional Medicine for South East Asian Countries which had nine recommendations for cooperation, collaboration and mutual support among signatory countries, including the:

a. development of institutionalized mechanisms for exchange of information, expertise, and knowledge with active cooperation with WHO on traditional medicine through workshops, symposia, visit of experts, exchange of literature, etc.; and the

b. pursuit of a harmonized approach for the education, practice, research, documentation and regulation of traditional medicine and involvement of traditional medicine practitioners in health services.

During the Sixty-seventh Session of the SEARO Regional Committee held in Dhaka, Bangladesh, September 2014, a resolution on Traditional Medicine: Delhi Declaration was discussed (SEA/RC67/11). This resolution recommended, among others, for the revised HerbalNet to be continuously updated for information exchange; the development of research methodology to evaluate quality of care; and to facilitate the integration of traditional medicine into conventional health systems.
Global

In Africa, there have been a number of developments in traditional medicine, with 2001-2010 being declared by the African Union as the Decade for African Traditional Medicine. The goal is to bring together all the stakeholders in an effort to make safe, efficacious, quality, and affordable traditional medicines available to the vast majority of Africans. In 2008, the African Network for Drugs and Diagnostics Innovation (DNDi) was launched whose goal is to promote and sustain African-led product R&D innovation through the discovery, development and delivery of affordable new tools, including those based on traditional medicines. 46

A number of research studies have been conducted to investigate the state of R&D in traditional medicine in specific African countries. In 2011, a research was done to look into the strategic plan and road map set up by the Government of Cameroon for the organisational framework and research platform for the practice and development of traditional medicine, and the global partnership involving the management of traditional management in the country. 47 In the same year, a study was also conducted in Nigeria to examine the research pattern in medicinal plants and traditional medicine practices with a view of determining how the country fared in herbal medicine research and development and the implications of the findings on the country’s health care system. 48

In Europe, a research network for complementary and alternative medicine (CAM) was established. It is called CAMbrella and consists of 16 partner institutions from 12 European countries. It conducted a research program which examined the situation of CAM in Europe between 2010 and 2012, and covered the following areas: terminology; the perspective of citizens on CAM; patients’ perspectives; providers’ perspective; and global perspective. It aims to evaluate the conditions underpinning CAM use in Europe and develop a roadmap for future European CAM research. 49

2 PROMOTING RESEARCH AND DEVELOPMENT

2.1 Supporting governments to develop or improve national health research programmes

Regional

Thailand

The National Science and Technology Development Agency (NSTDA) of Thailand and its centers have successfully created an alliance of universities, industry and government to link science to business and deliver research and innovation based on industrial needs. 50 Although NSTDA is not dedicated solely to the health sector, a large part of its activity is the conduct of R&D in the area of biotechnology. NSTDA makes use of 3 approaches to support innovation: clustering, public-public partnerships, and public-private partnerships.
India

In India, its 2011 National Health Research Policy has the following objectives: 51
- Identify priorities for effective and ethical health research in accordance with national health agendas and global commitments such as MDG and IHR.
- Foster inter-sectorial coordination to promote innovation leading to effective translation to indigenous production of diagnostics, vaccines, therapeutics, and medical devices etc.
- Focus on the vulnerable, the disadvantaged & the marginalized sections of society.
- Strengthen national networks
- Set strategies and mechanisms to assess the cost effectiveness and cost benefits of health interventions.
- Create, nurture human resources and infrastructure, encourage international collaborative research which contributes to national health.

In addition to the National Health Research Policy, India also has a number of related policies and bills which promotes its national health research programme. These include:
- Food Safety and Standard Amendment Bill 2014 introduced in Rajya Sabha
- The Indian Medical Council Amendment Bill 2013
- The Drug and Cosmetics Amendment Bill 2013
- The National Commission for Human Resources for Health Bill, 2011
- Biotech Authority Bill (2013) Global

A comprehensive listing of the different institutions/organizations providing support to national health research programs and its components and the mechanisms through which various forms of support are provided was prepared by the WHO Secretariat as a background document for the open-ended meeting in November, 2012. 52

During the III Meeting of BRICS Health Ministers in Cape Town on 7 November, 2013 a communiqué was released summarizing the important decisions reached during the meeting. 53

Two of the items listed in the communiqué were related to GSPA-PHI and the promotion of health R&D in BRICS countries, namely:

a. Reiterated their support for the full implementation of the WHO GSPA-PHI which gave rise to the Consultative Expert Group on Research and Development, and, in this context, drew attention to WHA Resolutions WHA66.22 and WHA65.24 with specific reference on demonstration projects. Acknowledged the value and need for experience and knowledge sharing. Urged BRICS countries to fully participate in the process of implementation of the identified projects through the establishment of networks and expert committees.

b. Focused on the unique strength of BRICS countries such as capacity for R&D and manufacturing of affordable health products and capability to conduct clinical trials. Called for enhanced cooperation in application of biotechnology for health benefits for the population of BRICS and other developing countries.
2.2 Promoting upstream research and product development in developing countries

Regional

Among the new mechanisms for upstream R&D collaboration and resource sharing is the use of open source infrastructure. An example is the Open Source Drug Discovery Infrastructure (OSDDI) which is an initiative led by India’s Council on Scientific and Industrial Research. A more detailed description of this initiative is presented in Section 4.3. In Bangladesh, there are 15 companies engaged in the production of Active Pharmaceutical Ingredients (APIs). However, only few of these companies have full-fledge R&D Laboratories for the development of APIs. Most of them are manufacturing under technology transfer either from India or China.

Global

Another type of upstream platform which has been implemented is that of the Structural Genomics Consortium (SGC).

The crystallization facility of the TB Structural Genomics Consortium is one of nine P50 structural genomics centers sponsored by the US National Institutes of Health. It provides TB consortium members with automated crystallization, data collection, and basic molecular replacement structure solution up to bias-minimized maps. In contrast to venture capital-funded commercial enterprises, the TB consortium facilities are decentralized and aim to develop high-throughput crystallography methods and automation on a comparatively small budget. In addition to financial constraints, the logistics and organization of a production environment differ considerably from academic settings. The TB Structural Genomics Consortium crystallization facility may thus provide a model for cost-effective, efficient high-throughput crystallography. The SGC contributed 29.6% of the global output of novel human protein target structures in 2009. These research outputs are free from restrictions on use and are not covered by intellectual property.

2.3 Improving cooperation, participation and coordination of health and biomedical research and development

Regional

The South East Asia Infectious Disease Clinical Research Network (SEAICRN), set up in 2005, is a collaborative partnership between hospitals and research institutions within Thailand, Viet Nam and Indonesia, the National Institutes of Allergy and Infectious Diseases (USA) and the Wellcome Trust (UK). It was created in order to develop the necessary partnerships in South East Asia in order to:

a. conduct collaborative clinical research that addresses emerging threats;
b. increase evidence-based scientific knowledge; and
c. directly contribute to improving the clinical management of infectious diseases of public health importance.
In 2011, the ASEAN-NDI was launched with the following objectives:

1. To develop projects leading to the discovery and development of novel drugs, vaccines, and diagnostics for tropical and other diseases carried out by teams of collaborating investigators and institutions in the network using knowledge management principles;
2. To provide a knowledge management platform and framework for scientific, legal and ethical support that promote investment in projects and partnerships for the discovery and development of pharmaceutical products; and
3. To facilitate creation of South-based cross-border institutions like public private partnerships, networks of academic institutions and not-for-profit foundations, focusing on, and dedicated to, innovation for discovery and development of drugs and diagnostic tests in ASEAN network members and the ASEAN dialogue countries.

The network is an initiative of ASEAN and is supported by the World Health Organization (WHO) TDR.

**Global**

Another Asian network established in 2009 is the Chinese Network for Drugs and Diagnostic Innovation, founded with the support of WHO/TDR, China’s CDC and the Ministry of Science and Technology. The participants include major universities, research institutes, hospitals, multinational pharmaceutical companies and biotech companies.

Its mission is:

1. To establish a network that shares scientific information and technical resources to leverage product R&D activities nationwide;
2. To develop workable mechanisms by which public-private partnerships in neglected diseases can flourish in China; and
3. To assist in intellectual property rights protection and advance legitimate interests of the network members.

Among the initial activities of the network were the conduct of an R&D landscape mapping and the organization of an international workshop on quality in clinical research.

The establishment of the African Network for Drugs and Diagnostics Innovation (DNDi) in 2008 was mentioned earlier in Section 3.1.3.2 of this report. Its vision is to create a sustainable platform for African research and development innovations to address Africa’s health needs. Its primary objective is to promote and support health product R&D led by African institutions for diseases of high prevalence in the continent. The expected outcome is the discovery, development and delivery of affordable new health tools including those based on traditional medicine, as well as the development of capacity and establishment of centres of research excellence.
In the Americas, the HTA Network of the Americas (RedETSA) was launched in June 2011. It has members from 13 countries and 25 institutions, with PAHO serving as the network Secretariat. It consists of experts from Region’s collaborating centers and reference institutions and aims to improve the ability of member countries to justify decisions on innovation, and the adoption, development, and use of health technologies in health systems.

2.4 Promoting greater access to knowledge and technology relevant to meet public health needs of developing countries

Regional
The Indian Council of Medical Research (ICMR) created history in February 2007 when India became the first and only low-income country in the world with a national subscription to The Cochrane Library. This initiative of the ICMR to purchase a national license was widely hailed as an exemplar of responsible leadership in health-research governance, as it gave all people in India with an internet connection free access to the online collection of reliable evidence-based resources to aid health decisions. The increased use of the resources in The Cochrane Library over the three years of the national provision led to the ICMR renewing the subscription for India-wide free access for a further three years to January 2013, with extension after this period being strongly advocated.

WHO/SEARO publishes the WHO South East Asia Journal of Public Health which provides an avenue to scientists for publication of original research work so as to facilitate use of research for public health action. The scope of the Journal is broad and includes original research articles on public health, primary health care, epidemiology, health administration, health systems, health economics, health promotion, public health nutrition, communicable and non-communicable diseases, maternal and child health, occupational and environmental health, social and preventive medicine which have potential to promote evidence-based public health action in the South-East Asia Region. The Journal also includes editorial, commentaries, perspectives, state of the art reviews, research briefs, policy and practice, reports from the field, public health classics, letters to the editor and book reviews.

A disease which remains to be a continuing problem especially in the Greater Mekong sub-region (GMS) is malaria. An initiative which aims to put together a comprehensive document which presents updated data on the malaria situation in the Region, its epidemiology, researches conducted and the progress of various programs and interventions implemented is the Mekong Malaria series (Mekong Malaria I, II and III).

Global
The Global Health Observatory (GHO) is the World Health Organization’s (WHO) gateway to health-related statistics from around the world providing access open health data and statistics. The GHO also issues analytical reports on priority health issues, including the World Health Statistics annual publication, which compiles statistics for key health indicators. Aside from the GHO being maintained by the WHO headquarters in Geneva, some WHO regional offices like PAHO, EMRO, WPRO, and AFRO have their own health observatories. HINARI (Health Inter Network Access to Research Initiative) Access to Research in Health Programme provides free or very low cost online access to the major journals in biomedical and
related social sciences to local, not-for-profit institutions in developing countries. Launched in 2002, today it has a base of up to 400 publishers offering more than 51,000 information resources. The country classification into groups is done based on total GNI (World Bank definition), United Nations Least Developed Country List (LDCs) and Human Development Index (HDI). Group A includes Bangladesh, Bhutan and Timor Leste who get free access and Group B include Maldives and Sri Lanka which pay a fee.  

HRWeb is an online information sharing platform driven by information uploaded by people. There is a drive to sustain dynamic flow and improvement of sharing like in the PAHO region, with the International Clinical Trial Database (ICTRP) into HRWeb to provide a one-stop shop repository with descriptors of national health research systems.

2.5 Establishing and strengthening national and regional coordinating bodies on research and development

Regional

Most SEAR Member States have a specific national coordinating body for health R&D. This was identified during the country presentations at the regional meeting to assess GSPA-PHI progress held in Bangkok in December 2014. A summary of the national coordinating bodies for health R&D of each country is presented in Annex 4.

At the regional level, a current initiative related to the coordination of health R&D activities among different countries is the establishment of the ASEAN-NDI which was described in Section 2.3. ASEAN-NDI launched its Strategic Business Plan in June 2013. The development of the document was guided by two other important documents, the ASEAN Plan of Action on Science and Technology (APAST) and the Blueprint for the ASEAN Socio-cultural Community.

Global

One of the specific actions listed under the sub-element on establishing and strengthening national and regional coordinating bodies on R&D is to facilitate the dissemination and use of R&D outcomes. This specific activity is embodied as one of the 4 strategic directions of the Canadian Institute of Health Research (CIHR) Strategic Plan for 2013-2014, which is to accelerate the capture of health and economic benefits of health research. Over the next five years, CIHR will build effective collaborations by: (1) facilitating and strengthening partnerships between researchers and knowledge users and between CIHR and a variety of organizations so that the impact of research is maximized; (2) supporting evidence-informed policy making to improve health and the health system at both the provincial and federal levels; (3) facilitating innovation and commercialization by creating incentives for health researchers to work with private sector partners to translate health research findings into improved health products, technologies and tools for Canadians; and (4) implementing citizen engagement initiatives.
3 BUILDING AND IMPROVING INNOVATIVE CAPACITY

3.1 Building capacity of developing countries to meet research and development needs for health products

Regional

- One of the partnerships developed for capacity building in health research is between the Health Economics and Financing Programme of the London School of Hygiene and Tropical Medicine and three research partners in South Africa and Thailand to strengthen health economics-related research capacity. In Thailand, individual capacities were built through post-graduate training and the partner institution developed this as part of a package aimed at retaining young researchers at the institution. In South Africa, local post-graduate teaching programs were strengthened, regular staff visits/exchanges initiated and maintained and funding secured for several large-scale, multi-partner projects. This study has shown that it is possible for long-term north-south partnership commitments to yield fruit and to strengthen the capacities of public health research and training institutions in less developed countries.

- A research and capacity building partnership between TDR, the Ecosystem and Human Health Program of Canada’s International Development Research Centre (IDRC) enabled 6 research institutions in India, Sri Lanka, Indonesia, Myanmar, Philippines, and Thailand to conduct research on dengue prevention.

- EDCTP and TDR are currently jointly awarding clinical research fellowships under their Clinical Research and Development Fellowship Scheme. It is open to researchers from low- and middle-income countries. For SEAR, eligible applicants to this training grant are nationals of Indonesia, India, Pakistan, Sri Lanka and Timor Leste. Fellowships are awarded to acquire experience and develop skills for conducting clinical trials outside of an academic or public sector setting.

Global

TDR has always been the leading institution to actively promote and foster individual, institutional and partnership development in order to win against infectious diseases of poverty. However it has re-prioritized its work in low and middle income countries to achieve its goal of access to knowledge and increasing research capacity. To do this TDR has identified 6 specific objectives, namely:

a. Analyze gaps and needs for agenda setting in research and capacity building;
b. Facilitate translation of evidence into action;
c. Strengthen capacity to conduct high quality interdisciplinary research
d. Promote leadership in health research
e. Foster harmonization and alignment of efforts for global health research and goals
f. Engage with key stakeholders around research and capacity needs
Other organizations which have been created at the global level as mechanism to promote and support research capacity strengthening are COHRED and the Global Forum. The Global Forum was created in 2007 to maintain a global policy focus on and monitor investments in building research capacity of low and middle income countries. COHRED and the Global Forum were merged in 2011.

There is a general agreement in the global community that in order to be effective, research capacity strengthening must involve a systems approach at country level, balancing long-term investments at 3 levels.

1. The individual investigator, in relation to the training and research support provided to them;
2. The institutions and organizations in which they work; and
3. The national and regional health research systems that can provide a supportive environment for sustainable growth and scaling up of a country’s capacity for health research

3.2 Framing, developing and supporting effective policies that promote the development of capacities for health innovation

Regional

One of the specific actions under this sub-element is the establishment and strengthening of regulatory capacity in developing countries. During the 32nd Session of the WHO South-East Asia Advisory Committee on Health Research held in Bangkok in Oct. 2011, it was reported by the sub-committee on drugs and vaccine development that SEARO has supported strengthening the capacity of National Regulatory Authorities (NRAs) in Bangladesh, India, Indonesia, and Thailand. Out of these Member Countries India, Indonesia and Thailand have well established vaccine production capacity with Bangladesh emerging as one... Each NRA has to have a standard quality system. Although NRAs of the three vaccine manufacturing countries are well in place, harmonization of the NRAs is still a tough challenge. The EU has recently developed a matrix on harmonization which can be used as reference for the SEARO Region.

The second set of specific actions under this sub-element of GSPA-PHI relates to the development and retention of human resources for health research. While there are a number of literature published at the regional or even at the country level on human resources for health in general, there is hardly any material specifically on policies related to human resources for health research in particular

Global

The Human Resource for Health Research (HR-HR) initiative, first of its kind, attempts to bring a holistic perspective to the issue of human resources for health research. The initiative was spearheaded by seven partners: AMREF, AfHRF, COHRED, ACOSHED, EQUINET, Global Forum for Health Research and IDRC, that came together in 2004 to look at specific human resource needs and challenges to overcome to improve health research in developing countries. The HR-HR expert
meeting was held on July 2-5, 2006 with the purpose contributing new thinking to the improvement of human resources for health research in low and middle income countries. Expert consultations were held in the four HR-HR themes:

- Health Research environment
- How networks and networking can improve health research
- Communities and their role in shaping health research agendas
- Communication and Knowledge translation approaches to improve the effectiveness of health research

In terms of specific support schemes for human resources for health research, TDR has developed such schemes around its three strategic functions:

a. Research capacity strengthening – supporting training, leadership development and project-related capacity building to strengthen the ability of countries and regions to respond to their own research needs;

b. Gap analysis for agenda setting – promoting evidence-based priority setting to identify emerging needs in research and capacity strengthening; and

c. Partnership and engagement – collaboration with WHO, TDR co-sponsors and partners for harmonization and alignment with global health goal

To realize these 3 strategic functions, the following support schemes will be pursued:

a. Regional small grants in collaboration with WHO regional offices to support priority research and knowledge management activities;

b. Advanced research training including degree training, re-entry grants and career development fellowships in collaboration with public and private partners;

c. Short-term learning to support individual or group training linked to research projects, special initiatives or institutional development programmes;

d. Institutional programme-based support to selected institutions to acquire sustainable critical research and training capabilities, including regional hubs; and

e. Research networks and working group to strengthen collaboration in research, training, production of analytical reports and build consensus of protocols around areas of common interest
3.3 Providing support for improving innovative capacity in accordance with the needs of developing countries

Regional

SEAMEO TROPMED Network, a regional cooperation network established in 1966 for education, training and research in tropical medicine and public health under the Southeast Asian Ministers of Education. It has 5 objectives as follows:

a. To support research on endemic and emerging diseases associated with changing environment
b. To advocate relevant health policies that are compatible with equitable and sustainable development
c. To empower communities with the necessary knowledge and skills for understanding and finding solutions to health problems
d. To encourage the use of traditional and modern-day tools for health promotion and disease prevention whenever and wherever applicable and
e. To minimize the economic burden of health.

The establishment of the ASEAN NDI is another recent development in the region which contributes to building capacity of developing countries to meet R&D t needs for health products. The establishment and the role of ASEAN NDI has been discussed in a number of sections in this report.

Global

Strengthening Pharmaceutical Innovation in Africa is a long-term capacity building programme created by African research and political leaders to craft strategies build skills, to engage in pharmaceutical innovation and access to medicines for the benefit of the Africans as mentioned above in sub-element 1.2.

One of the specific actions under this sub-element in the strengthening of health surveillance and information systems. A leading initiative in this area is Health Metrics Network (HMN). HMN’s mission is to mobilize partners to strengthen health information systems and to increase the availability of information for decisions to improve health outcomes in countries. Established in 2005, it is the first global partnership dedicated to strengthening national health information systems. HMN operates as a network of global, regional and country partners. As a country-owned and partner-driven platform, it assesses health information systems and sustainably improves them, through the use of the HMN Framework. HMN has done assessments and provided technical support for the strengthening of the health information systems of several countries.
3.4 Supporting policies that will promote innovation based on traditional medicine

**Regional**

As per the WHO 2014-2023 Traditional Medicine Strategy for SEAR most notable progress has been the introduction of T&CM policies by five member states and putting in place a national policy by each member except Timor Leste. In herbal monographs while another 4 countries updated their existing pharmacopoeia. Six countries have lists of essential traditional medicine. India and Indonesia are contributors to the International Regulatory Cooperation for Herbal Medicines (IRCH).

**Global**

Annex A of the WHO Traditional Medicine Strategy lists several examples of notable T&CM initiatives in different parts of the world. Among the initiatives related to promotion of innovation based on traditional medicine are as follows:

- In AFRO, progress has been made in policy development and provider education. The number of African countries with national T&CM policies increased from 8 in 1999/2000 to 39 in 2010. Country regulatory frameworks increased from 1 in 1999/2000 to 28 in 2010, including various instruments such as the code of ethics and the legal framework for T&CM practitioners.

- By 2010, 22 African countries were conducting research on traditional medicines for malaria, HIV/AIDS, sickle-cell anemia, diabetes and hypertension using WHO guidelines.

- Guidelines for the protection of intellectual property rights (IPR) and traditional medicine knowledge (TMK) have been developed. By 2010, 6 countries had national tools for IPR and TMK protection versus 0 in 1999/2000.

- In EMRO, 7 Member States have national T&CM regulation. The Council of Arab Health Ministers is discussing a project for harmonizing legislation on T&CM in the Arab countries.

- In EURO, T&CM legislation is being developed with the intention of adopting a harmonized approach to the regulation of herbal medicines across the European Union.

3.5 Developing and implementing incentive schemes for health-related innovation

**Regional**

Thailand provides incentives to both individual researchers and the private sector and industries to stimulate research and development. For individual researchers, annual prize and awards are given by TRF, NRCT AND NSTDA. Science and technology post-graduate students as well as young
scientists are provided scholarship. Co-funding are also provided for joint projects between supervisors and research institutes.

For the private sector and industries, the following incentives are provided:
- Tax deduction for R&D expense and depreciation cost
- Tax exemption for imported equipment’s and corporate income tax
- Cash and soft loan
- Joint venture with technology transfer
- Buddy/mentor system
- Consultancy system
- Services on S&T

In India, the Biotechnology Industry Research Advisory Council (BIRAC), to date, has supported 240 companies for 360 projects with a funding support of approximately 100 million USD. From the private sector, the commitment for funding support is worth of 120 million USD. Out of these, 77 projects involved Industry-Academia collaborations which have delivered 17 affordable products and 11 new technologies creating 24 intellectual property and 3 bio-industrial facilities.

Drug regulation imposes standards on the products of health related research and development. It is intended to protect patients by ensuring the quality, efficacy and safety of new pharmaceuticals and biological. In 2009, a study was conducted for WHO’s Commission on Intellectual property Rights, Innovation and Public Health (CIPIH) to address the issue of the impacts of drug regulation on incentives for R&D of new drugs and vaccines. It examined the ways in which regulatory framework affect the incentives for pharmaceutical innovation using ASEAN member countries as a case study.

Global

In the area of developing antibacterial drugs, the following policies to create incentives have been proposed:

a. Financial incentives – tax credits; advanced market commitments for purchase; payments for conservation

b. Priority review vouchers – US legislation enacted in 2007 aimed to provide an incentive to develop drugs for neglected tropical diseases by allowing the US FDA to grant companies that obtain approval for a drug for a tropical disease a one-time, transferable priority review voucher for an unrelated future drug.

c. Orphan drug incentives – for example, the 1983 US Orphan Drug Act offers extended tax credits and guarantees 7 years of market exclusivity to developers of drugs for rare conditions that affect <200,000 patients in the US. The US Congress could extend the act to cover all new antibacterials or enact a law specifically for antibacterials for certain multi-drug resistant infections

d. Liability exemption – exempt manufacturers from liability associated with their antibacterials, as with the case of vaccine manufacturers
e. Broadening the scope of anti-bacterial patents – patents could be awarded for new “functional resistance groups” rather than for single molecules, where the functional resistance group includes all molecules that are active against bacteria that share a common and novel genetic basis of resistance.

f. Public-private partnerships (PPPs) – PPPs reduce participant’s costs and risks by sharing funds and expertise among the public, the philanthropic and private sectors.

g. Encouraging strategic antibacterial reserves – Incentive payments for antibacterials could be linked to government-set conservation and resistance targets. Disease incidence and rates of emerging resistance can be tracked and used to set public health goals.

4 TRANSFER OF TECHNOLOGY

4.1 Promoting transfer of technology and the production of health products in developing countries

In 2011, the results of a WHO study on “Improving access to medicines in developing countries through technology transfer related to medical products and local production” was published. The study had three objectives, namely to provide:

- a description of the landscape of local production of drugs, relevant investment promotion and related transfer of technology;
- an outline of current and recent initiatives (taking place within the past 5–10 years); and
- an identification of gaps and preliminary assessment of the initiatives.

Among the important findings of this study are as follows:

- There is a wide range of actors transferring technology to local producers, including individuals, non-profit-making institutions, multinational pharmaceutical companies and major public institutions.

- There is a wide variation in the scale and level of technical sophistication of technology transferees. They include large firms with annual revenues of about US$ 1 billion and include all stages of production for both drugs and vaccines.

- India-based manufacturers of both drugs and vaccines were the most frequent participants of technology-transfer initiatives, followed by China and Brazil. Technology was also transferred to less advanced generics firms in smaller or less developed countries with some concentration East Africa, particularly for anti-malarials.
In addition to technology transferors and transferees, local production initiatives often involve third parties of “facilitators” who may play a variety of roles including research; advocacy; coordination; funding; connecting or screening potential partners; brokering agreements; increasing absorptive capacity; advising; providing additional incentives; and creating a conducive policy environment.

Among the technology receiving countries, government actors played a wide range of roles and initiatives involved Ministries of Health, the National Drug Regulatory Authority, trade, industry, science and technology and education.

Three multi-lateral organizations provide direct support (i.e., activities aimed specifically at local producers, including technology transfer, training and financing) These are WHO, UNIDO and the International Finance Corporation of the World Bank Group (IFC).

Seven multilateral organizations provide indirect support to local production efforts such as policy advice, capacity building, institutional strengthening and analysis. These are UNIDO, UNCTAD, World bank, UNDP, WHO, UNICEF and the African Union.

Several governments from north and south, most notably Brazil, the EU, Germany, Thailand, UK and the US, have facilitated local production efforts in other countries either directly through technology transfer, training or funding, or indirectly through analysis and policy advice.

A major area for technology transfer is in vaccine production. WHO, together with governments, the pharmaceutical industry and other stakeholders has been implementing the 2006 Global Pandemic Influenza Action Plan which involved the transfer of technology necessary to build production capacity for influenza vaccines in developing countries. To meet this end, the influenza vaccine technology transfer initiative was launched in 2007. Since 2008, WHO has provided 11 seed grants to manufacturers in low and middle-income countries to establish or strengthen their capacities for pandemic influenza vaccine production. An important part of this project was the establishment of a technology platform at the Netherlands Vaccine Institute (NVI) which provided training and technology transfer to participants from developing countries.

In 2010, a meeting of vaccine technology transfer stakeholders was held at WHO, Geneva to review the technology transfers that have taken place over the last two decades. The meeting identified trends and conditions for success, reviewed different models and drivers for technology transfer. The main conclusions from this meeting were as follows:

- Technology transfer to developing countries has contributed significantly to increase in vaccine supply, access and affordability.

- Establishing local vaccine manufacturing is not necessarily cost effective, Thus establishment of a vaccine policy by countries may assist countries in identifying how and when to consider local production.

- There is a changing dynamic in vaccine technology transfer, with joint ventures, acquisitions, and establishment by multinational manufacturers of subsidiaries in
developing countries. The establishment of research-based entities developing and providing new vaccines may squeeze existing 'generic' manufacturers out of the market. The latter will need to invest in R&D to remain competitive.

- The biggest barrier to vaccine technology transfer, perceived by both the technology recipients and donors, is lack of R&D capacity in developing countries. A failure by manufacturer to invest and government to create an environment will impact optimality of technology transfer.

- For technology transfer to be attractive and successful a win-win condition is required which is facilitated by a commitment from the government to support the technology transfer, and/or a large local or regional market.

Regional

Of the 11 WHO grantees for technology transfer in influenza vaccine development, 3 were from SEAR. Table 2 shows a listing of these countries with the corresponding manufacturers, ownership (public/private) and type of technology transferred.

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>MANUFACTURER</th>
<th>TECHNOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>Serum Institute of India (private)</td>
<td>Egg-based technologies: 1) whole virion aluromated inactivated vaccine; and 2) live attenuated influenza vaccine using WHO sub-licensed Russian technology</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Bio Farma (public)</td>
<td>A fill-finish facility and upstream vaccine antigen production unit though adoption of Japanese technology for seasonal vaccine: split egg-based product</td>
</tr>
<tr>
<td>Thailand</td>
<td>Government Pharmaceutical Organization (public)</td>
<td>Egg-based technologies: 1) Establishment og an egg-based split inactivated seasonal vaccine process; and 2) live attenuated influenza vaccine using WHO sub-licensed Russian technology</td>
</tr>
</tbody>
</table>

Source: Extracted from Table 2, Francis, D.P and Grohmann, G. 85

The experience gained by India in manufacturing the H5N1 vaccine as part of the WHO grant was used to develop a live attenuated influenza vaccine (LAIV) during the outbreak of the AH1N1 influenza pandemic in 2009. Serum institute of India (SII) took less than 12 months to develop and market its LAIV intranasal vaccine from receipt of the seed strain from WHO. As of November 2010, over 2.5 million persons have been vaccinated with Nasovac with no serious adverse reactions.
after 3 months’ post-marketing surveillance. The product has been submitted for prequalification by WHO for purchase by UN agencies.  

In Thailand, the domestic production of seasonal influenza vaccine was mandated in 2005, under the National Strategic Plan for Pandemic Influenza Preparedness. The government then decided to provide funds to establish an industrial-scale influenza vaccine production plant and gave responsibility for this project to the Government Pharmaceutical Organization (GPO). In early 2009, during the second year of the project, GPO started to develop a pandemic live attenuated influenza vaccine (PLAIV) against the influenza A(H1N1) virus. By December 2010, the H1N1 PLAIV had successfully completed Phase 2 clinical trials and was awaiting registration approval from the Thai Food and Drug Administration. The GPO has also started to develop H5N2 PLAIV which was expected to enter clinical trials in January 2011.  

In Indonesia, the triggering factor for vaccine development was avian influenza A(H5N1) which spread in humans in 2005 with a very high case fatality rate of 80%. In response, the government embarked on a program for influenza preparedness which included the domestic production of influenza vaccine. This was entrusted to Bio Farma which adopted the strategy of developing trivalent influenza vaccine capacity in order to be able to convert immediately to monovalent production of up to 20 million pandemic doses for the Indonesian market, upon receipt of the seed strain from WHO. After producing 3 consecutive batches and conducting successful clinical trials, the product was licensed by the Indonesian national Regulatory Authority and was distributed commercially for the Hajj Program in 2009. Bio Farma is now advancing with the development of upstream processes to produce its own bulk for seasonal and pandemic use.  

In addition to the influenza vaccine, technology transfer has also been done for other diseases. For example, the International Vaccine Institute (IVI) transferred technology for the inactivated whole cell cholera vaccine (ORC-Vax VaBiotech) which was not WHO prequalified but was very cheap (at US$1 per dose) when compared to the WHO prequalified Dukoral (at 40 euros for 2 doses). IVI chose to undertake this technology transfer based on the need for a safe, high quality and affordable vaccine. Steps were taken to improve the safety and quality of the vaccines through reformulation and quality control. Phase III clinical studies were undertaken with positive results and technology transfer of the vaccine was undertaken to Shantha Biotechnics, of India. Through 2 week training at IVI, successful scale up at Shantha followed and the vaccine was licensed in February 2009. A subsequent step involved ToT of quality control assays for this vaccine to VaBiotech, Viet Nam.  

IVI likewise transferred technology for the Typhoid vaccine to Shantha Biotech which IVI chose to undertake in order to make available an affordable, high quality, safe and efficacious typhoid fever vaccine which could be targeted at populations most at risk from typhoid infection and could be delivered with EPI vaccines, clinical trials for this vaccine are planned for 2011.  

Another Indian institution, the Serum Institute of India was also the recipient of 5 technology transfers for vaccine manufacturing, namely: measles, mumps and rubella from the Institute of Immunology in Zagreb; Hib vaccine from NVI; MenA vaccine with PATH-WHO; rabies monoclonal antibody through MBL; and HepB vaccine from Rhein Biotech. The same institute was the recipient of the WHO grant for influenza vaccine production described earlier.
A comprehensive study which assessed India’s role in global health research and development was published by The Results for Development Institute (R4D) in 2012. Among the important findings of this study are the following:

- The various elements required for biomedical innovation like trained human resources with the right mix of skills; publicly supported research with strong links to industry; financing for product development; access to technology; rigorous but supportive regulation; functioning infrastructure and markets for products are in place in India in varying degrees, but important gaps remain;

- India’s vaccine R&D capacity is growing. The leading firms have moved from process development and incremental innovation in combinations and formulations, to the development of new vaccines. Across the industry, new vaccines against rotavirus, Japanese encephalitis, typhoid fever, malaria, rabies and influenza are in clinical development. Many more project are at earlier stages including those for dengue, chikungunya and cholera.

- Unlike the vaccine companies, Indian drug firms show little interest in developing new drugs against neglected diseases, although they remain to be important suppliers of affordable medicines for India as well as other low and middle-income countries.

- There is considerable potential for India to contribute to the development of new locally adapted diagnostics for both infectious and non-communicable diseases. Although the R&D capacity of India’s test developers like that of its drug and vaccine industries lag behind international leaders, these firms have the expertise to bring to market tests based on established platforms relatively cheaply when appropriate biomarkers are available. A few Indian firms may also be able, with technical and financial assistance, to develop new diagnostic platforms that are more affordable and require less infrastructure than existing products.

Global

In Table 2, the list of WHO grantees from SEAR for technology transfer in influenza vaccine development was listed. The 8 other grantees from other regions are listed in Table 3.

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>MANUFACTURER</th>
<th>TECHNOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>Instituto Butantan (public)</td>
<td>Egg-based inactivated split and/or whole virion H5N1 with adjuvant, based on transfer of seasonal production technology</td>
</tr>
<tr>
<td>Mexico</td>
<td>Birmex (public)</td>
<td>Egg-based split vaccine. Establishment of a blending, filling and packaging facility as a first step using imported antigens</td>
</tr>
<tr>
<td>Country</td>
<td>Organization</td>
<td>Description</td>
</tr>
<tr>
<td>-------------------------------</td>
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<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>Institute of Vaccines and Medical</td>
<td>Small scale production facility for the production of egg-redived whole virion and alum adjuvanted H5N1 and H1N1 influenza vaccines, and a small scale chicken farm for egg supply.</td>
</tr>
<tr>
<td></td>
<td>Biologicals (Public)</td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>Vacsera (public)</td>
<td>Small scale facility to produce egg-derived whole virion influenza vaccine</td>
</tr>
<tr>
<td>Islamic Republic of Iran</td>
<td>Razi Institute (public)</td>
<td>Egg-based influenza vaccines in small-scale facility</td>
</tr>
<tr>
<td>Republic of Korea</td>
<td>Green Cross Corporation (private)</td>
<td>Establishment of dedicated plant for alum adjuvanted whole virion H5N1 influenza vaccine</td>
</tr>
<tr>
<td>Romania</td>
<td>Cantacuzino Institute (public)</td>
<td>Pilot-scale production of seasonal egg-based inactivated split influenza vaccine</td>
</tr>
<tr>
<td>Serbia</td>
<td>Tortak (public)</td>
<td>Construction of a new filling department</td>
</tr>
</tbody>
</table>

Source: Extracted from Table 2, Francis, D.P and Grohmann, G. 85

In China, PATH has been active in capacity building for the Japanese encephalitis vaccine. In 2005, a new facility aimed to meet the production capacities for the needs of Asian countries which would meet WHO prequalification for the Japanese encephalitis vaccine was established. The facility was expected to start industrial runs in 2011. 88 Another company active in Tot in China is Sinovac which is one of the largest vaccine manufacturers in the country. The objective of Sinovac is to improve Chinese-produced vaccines to meet global standards. 88

4.2 Supporting improved collaboration and coordination of technology transfer for health products

Regional

Productive collaboration between the public sector laboratories and industry has been identified as a major positive factor for diagnostics development in India. A number of tests initially developed in the public sector have been successfully commercialized including tests for dengue and hepatitis C which were developed at the International Centre for Genetic Engineering and Biotechnology in New Delhi. 92

In the area of influenza vaccine production, technology and intellectual property transfer activities mediated by WHO have resulted in expanded production of live attenuated influenza vaccine (LAIV) in both India and Thailand using vaccines based upon the LAIV backbone developed by the Institute of Experimental Medicine in Russia. Coupled with the ground work established by WHO, high-performing partners, and local government support, this vaccine was ready in unprecedented time. 93
Global

Domestic influenza vaccine production in Mexico provides a good example of a successful collaboration between a state-owned and a multi-national company. In 2004, the Mexican government developed a plan for pandemic influenza preparedness which included local production of the influenza vaccine. To achieve this goal, an agreement was made between Birmex, a state-owned vaccine manufacturer and Sanofi-Pasteur, a private multinational company. Under this agreement, Sanofi Pasteur will establish a facility in Mexico which will produce antigen for up to 30 million doses of egg-based seasonal vaccine each year while Birmex will build a facility to formulate, fill and package the inactivated split-virion influenza vaccine. As of November 2010, the Sanofi-Pasteur facility was completed and the Birmex plant was under construction. In addition to intensive support from Sanofi Pasteur for transfer of technology, the project is supported by the Mexican Ministry of Health, complemented by Birmex’s own budget and grants for the WHO developing country influenza technology transfer project.

Working relationships established between the US Department of Health and Human Services (HHS) Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority (BARDA) and its partners have assisted in advancing influenza vaccine development at many different levels. In 2009, BARDA used its international capacity-building funds to establish a US$ 7.9 million cooperative agreement with PATH, which allowed the support of final developmental processes for an egg-grown influenza vaccine at the Institute of Vaccines and Medical Biologicals (IVAC) in Vietnam. The PATH-supported Phase I clinical trials from vaccine produced at IVAC were expected to be initiated by 2012. The close working relationship between BARDA, PATH, WHO and the Vietnam Ministry of Health has helped to assure that this project will be successful, and the egg-based production facility, which was partially funded through these collaborations, will be able to produce millions of doses per year of pandemic vaccine.

4.3 Developing possible new mechanisms to promote transfer of, and access to key health-related technologies

Regional

In 2010, a workshop entitled “Towards New Business Models for R&D for Novel Antibiotics” held in Uppsala, Sweden identified new approaches to reinvigorate antibiotic R&D efforts. Among the new approaches mentioned was open access resource sharing and open source innovation and example of which is OSDD for TB. This initiative was led by India’s Council on Scientific and Industrial Research and tapped into a network of universities, companies, contract research organizations and volunteers. Among the projects undertaken by OSDD was the collective effort to study the Mycobacterium tuberculosis genome in search of novel drug candidate projects. With over 4328 registered participants from 130 countries, the OSDD mustered numerous volunteer contributions needed to complete a remapping and annotation of the genome in just 4 months. Adding another dimension to its digital platform for scientific collaboration, the OSDD will launch an Open Access Small Molecules Repository comprised of acquisitions from existing libraries, dedicated synthesis efforts, and other contributions.

Another innovation is in the area of product development partnerships with the Drugs for Neglected Diseases Initiative (DNDi) being a successful pioneer in this area. The development of a
second anti-malarial combination, ASMQ (artesunate-mefloquine) resulted from south-south collaboration between Brazil’s Farmanguinhos and the Indian drug firm, Cipla. In bringing ASMQ to market, DNDi worked with the Indian Council of Medical Research and with the Kenya Medical Research Institute, both of which helped to shape antimalarial policy development through their efforts.  

Global

The US Department of Health and Human Services (HHS) has been involved in, and supported a lot of cooperative agreements with various agencies especially in the area of vaccine development. Since 2005, it has provided more than US$ 50 million for influenza vaccine development in low-resourced countries. The funding for this programme has been primarily through a cooperative agreement with WHO to support directly its capacity-building grants to government-owned or government-supported vaccine manufacturers in developing countries. A second cooperative agreement reached with the Programme for Appropriate Technologies in Health (PATH) was initiated to accelerate the completion of a current Good Manufacturing Practice production facility, to support facilities to obtain a reliable supply of eggs and to conduct clinical trials of influenza vaccine manufactured in Vietnam. This mechanism of utilizing cooperative agreements to support capacity building for vaccine development in low-resourced settings has been novel, unique and efficient since it has yielded fruitful returns for minimum investment.  

Another new mechanism implemented for technology transfer is the “hub” model. This was first applied to facilitate the WHO project of providing seed grants to 11 manufacturers in low and middle-income countries to establish or improve their capacity for pandemic influenza vaccine production. An influenza vaccine technology platform or “hub” was established at the Netherlands Vaccine Institute whose objective was to pool public sector knowledge and expertise on a generic pilot process for influenza vaccine production that could be transferred to and easily scaled up in developing countries. During the first two years of operation, a robust and transferable monovalent pilot process for egg-based inactivated whole virus influenza A vaccine production was established under international GMP standards. A course curriculum as designed including a 2-volume practical handbook on production and quality control. Four generic hands-on training were conducted which included 40 employees from 15 developing country manufacturers. The generic hub approach to technology transfer can be seen as complementary to the bilateral partnerships for domestic influenza vaccine production. Assessments made on this model have concluded that “technology transfer through the hub model works well, significantly builds vaccine manufacturing capacity in developing countries, and thereby increases global and equitable access to vaccines of high public health relevance”.  

Another example of a successful product development partnership is the Meningitis Vaccine Project in Africa. The vaccine, known as MenAfriVac was specifically targeted for use in low-income countries in Africa. Major partners in this project include the Gates Foundation which provided the funds, WHO, PATH, the US Food and Drug Administration’s Center for Biologics Evaluation and Research which transferred technology to the Serum Institute of India for vaccine production. These partnerships dispersed the multiple tasks of product development across a network of partners which are best suited for each task. During the first few weeks after the vaccine was in the
market in late 2010, more than 19 million people in Burkina Faso, Mali and Niger were vaccinated.

a. South-south innovation platforms. Examples of initiatives using this model are:

- European and Developing Countries Clinical Trials Partnership which facilitates Phase II and III clinical trials for drugs, vaccines and microbicides against HIV/AIDS, TB and malaria in sub-Saharan Africa. 97 Firms have increasingly recognized the advantages of outsourcing clinical trials to southern countries where patient samples are readily available, overhead costs are low and capacity to uphold clinical research standards is growing.

- African Network for Drugs and Diagnostics Innovation (ANDi) and its sister networks in Asia and the Americas which seek to promote regional networks that are locally owned. 46 By linking centers of excellence across Africa, ANDi may help build south-south partnerships where few have existed.

A recent activity in the area of antibiotic research was a one-day “Technical Consultation for New Antibiotics Development and preservation” held at the WHO Headquarters in Geneva on 13 May 2014. 98 The meeting brought together leading experts to present and discuss innovative models which foster the discovery and development of new antibiotics as part of the tool-kit to address challenges related to anti-microbial resistance. Among the models presented during this meeting were:

a. New Drugs for Bad Bugs (ND4BB) programme – a major public-private partnership effort to address bottlenecks in the discovery and development of new antibiotics launched by the Innovative Medicines Initiative in 2012 99

b. Antibiotic Health Impact Fund (aHIF) – this is designed to achieve two core goals: 100
   - The availability of effective, safe antibiotics over the long run; and
   - Access to such antibiotics by patients regardless of their income

c. A publicly financed global consortium for R&D to fight antibiotic resistance – a proposal which focused on creating a consortium to coordinate pharmaceutical innovation for antibiotics by taking concerted public sector action. Incentives to drive R&D would be applied through a hybrid model of push and pull financing. 101
5. APPLICATION AND MANAGEMENT OF INTELLECTUAL PROPERTY TO CONTRIBUTE TO INNOVATION AND PROMOTE PUBLIC HEALTH

5.1 Support information sharing and capacity building in the application and management of intellectual property

Regional

In order to build and strengthen capacity to manage and apply intellectual property in a manner oriented to public health needs and priorities of developing countries, a series of training activities were conducted in the Region. In 2013, the WHO Country Office for India and the Ministry of Health & Family Welfare, Government of India, jointly organized a colloquium on intellectual property rights for high-level policymakers in India from 17-20 September 2013 at New Delhi. The colloquium was aimed at enhancing knowledge of policymakers on how to optimally apply flexibilities of Trade-Related Aspects of Intellectual Property Rights Agreement (TRIPS) and adapt intellectual property protection measures to better promote public health. During the colloquium, the policymakers were familiarized with crucial concepts relating to intellectual property, trade and public health, followed by India-specific case studies of legal provisions, cases and national debates, with specific focus on compulsory licensing.

Another capability building activity conducted was a workshop on intellectual property, public health and environmental policy for Asia and the Pacific Region. It was held in 2012, and was conducted by WTO in collaboration with UNESCAP and the International Islamic University of Malaysia.

Global

A large number of training activities were also conducted at the global level, as well as in the other regions. Among the training conducted in 2014 were:

- “Global Advocacy: Social Movements and Market Transformation” – the Case of AIDS Drugs for All” Geneva, 20 February 2014
- “WTO-WIPO colloquium for teachers of intellectual property” organized by WIPO and WTO, Geneva, 16-27 June 2014
- “Advanced course on intellectual property for government officials” organized by WIPO and WHO, Geneva, 10-21 March 2014
- “Workshop on intellectual property and public health “ organized by the WTO Secretariat in collaboration with the Secretariats of WHO and WIPO and the Egyptian Ministry of Health and Population, Cairo, 4-5 June 2014
5.2 Providing technical support to policy processes to countries that intend to make use of the provisions of the Agreement on Trade-related Aspects of Intellectual Property Rights

Regional

ICMR is the premier autonomous organization of the Department of Health Research of India, for planning, coordinating and conducting biomedical research in India. Its mission is to promote biomedical research through its research institutes/centres as well as to sponsor and support extramural research so that the various technologies developed could be transferred to the industries for commercialization, thus making them accessible to society.103

WHO continues to provide technical support to countries in areas related to TRIPS and its applications. In Bangladesh, the conduct of a WHO-supported workshop on intellectual property and trade for health products is scheduled for 2015.55

Global

As part of the process of implementing the 5th element of the GSPA, WHO, WIPO and WTO are engaged in trilateral cooperation and published a study, “Promoting access to medical technologies and innovation: intersections between public health, intellectual property and trade”.104 The study has emerged from an ongoing programme of cooperation between these agencies and responds to an increasing demand, particularly in developing countries, for strengthened capacity for informed policy-making in areas of intersection between health, trade and IP, focusing on access to and innovation of medicines and other medical technologies. The need for cooperation and coherence at the international level has intensified over the past decade, as indicated by successive multilateral decisions which have been made. Policymakers increasingly need to understand the complex interplay between different disciplines, at a time when stronger analytical tools and improved data are available. An integrated approach can reinforce a dynamic, positive interplay between the measures that promote innovation and those that ensure access to vital medical technologies. While addressing the broader issue of innovation and access to the whole range of medical technologies, the study focuses mainly on the area of medicines for which most practical experience and data are available.104

5.3 Exploring and promoting possible incentive schemes for research and development on Type II and Type III diseases

Regional

During the December 2014 regional meeting on the assessment of GSPA-PHI progress, very few countries mentioned the promotion of incentive schemes for R&D on Types I, II and III diseases.
Sri Lanka offers triple tax incentives in the form of a deduction of 3LKR from the corporate tax of private companies, for every 1LKR invested in R&D, in collaboration with the government research institutes.\textsuperscript{105}

In India, OSDD initiative as mentioned in 4.3 is an example.\textsuperscript{106}

**Global**

An economic analysis of various R&D incentives for neglected diseases was done in 2012 by Dimitri.\textsuperscript{107} She considered three types of incentives—those based on pull factors, the push programs, as well as the hybrid initiatives which consider both pull and push incentives. Supporters and critics of these various incentive schemes have argued in favor of their relative merits and limitations, although the view that no mechanism is a perfect fit for all situations appears to be widely held. For this reason, the debate on the advantages and disadvantages of different approaches has been important for policy decisions, but is dispersed in a variety of sources. With this in mind, the aim of the paper was to contribute to the understanding of the economic determinants behind R&D investments for neglected diseases by comparing the relative strength of different incentive schemes within a simple economic model, based on the assumption of profit maximizing firms. The analysis suggests that co-funded push programs are generally more efficient than pure pull programs. However, by setting appropriate intermediate goals hybrid incentive schemes could further improve efficiency.

In 2013, Agitha presented alternative incentive models delinking research and development costs from the price of pharmaceutical products. An open access, collaborative research model with prize fund incentive delinking costs of R&D from product price was suggested. In addition, the need to shift issues related to pharmaceutical R&D from the trade fora to the human rights forum was also recommended.\textsuperscript{106}

6 Improving delivery and access

6.1 Encouraging increased investment in the health-delivery infrastructure and financing of health products

**Regional**

Among the specific actions under this sub-element is the prioritization of health care in national agendas. The 6\textsuperscript{th} National Health Assembly of Thailand which was held in June 2014 tackled 8 agenda items which include the national strategy on community health system, a crucial area in health delivery infrastructure. It also included the multidisciplinary collaboration on health care for humans, animals and the environment (One Health) which is highly relevant in the recent surge of zoonotic diseases like the avian flu.\textsuperscript{108}

In the case of India, the Prime Minister’s 17-point agenda to take the nation forward released recently included health reforms focusing on capability building for human resources.it involves deployment of male community health workers, setting-up of knowledge institutes in districts which at the same time will function in coordination with upgraded district hospitals, and a 3-year
B.Sc. course in community health. The country has also been encouraging health care investment and financing of health products by implementing speciality care models, CSR and medical tourism.

A boost to the health delivery infrastructure of Sri Lanka was the setting up of the National Control Laboratory (NCL) and Drug Testing Laboratory (DTL) under the Directorate General of Drug Administration. The laboratory equipments were procured by WHO with financial support from the Health, Population and Nutrition Sector Development Program (HPNSDP).

Global

There are several organizations which invest in health development. They include a diverse selection of national and multinational development agencies, international financial institutions, and science and technology agencies. Among the agencies investing most in developing health delivery infrastructure during the period 2007 – 2011 are the US NIH, Bill and Melinda Gates Foundation, European Commission, USAID, Wellcome Trust and Institut Pasteur. Government Development agencies like USAid and JICA channel aid funding to developing countries driven by aim to reduce poverty, affordable access and spread of awareness.

The Bill and Melinda Gates Foundation’s Global Health Division aims to harness advances in science and technology to save lives in developing countries. It works with partners to deliver proven tools including vaccines, drugs and diagnostics, as well as discover path-breaking new solutions that are reliable and affordable. Equally important is innovation on how health interventions are brought to those who need them most. The Foundation invests heavily in vaccines against infectious diseases and supports the development of integrated health solutions for family planning, nutrition and maternal and child health.

6.2 Establishing and strengthening mechanisms to improve ethical review and regulate the quality, safety and efficacy of health products and medical devices

Regional

Different SEAR Member States have different regulatory bodies and mechanisms for ethical review and regulation of the quality, safety and efficacy of health products. A description of such mechanism was presented by 7 of the countries in the region during the regional Meeting on the assessment of GSPA-PHI progress held in Bangkok in December 2014. These are summarized in Annex 5.

Global

In order to assess national drug regulatory systems, WHO has developed an assessment tool to strengthen national medicines regulatory and control capacity through an assessment of the drug regulatory system. Application of the tool enables countries to do the following: (1) review of the existing legal framework, regulations and control activities with regard to medicinal products, in order to assess the national regulatory capacity, (2) identify of gaps and the development of strategies to address these gaps, (3) identify of specific areas and activities for WHO’s technical
input. If used from time to time on the same national medicines regulatory authorities, it can monitor the results brought by a project. The methodology enables the assessor to apply this tool to multiple health products like medical devices, cosmetics, etc. 112

In the Americas, regulation is implemented by the Pan American Network for Drug Regulatory Harmonization (PANDRH). PANDRH was officially established in November 1999. Its members include drug regulatory authorities of all PAHO member states, representatives of the regional pharmaceutical industry associations (ALIFAR, FIFARMA), academia, consumer groups, professional associations and representatives from the five sub-regional trade integration groups within the Americas such as the ANDEAN COMMUNITY, CARICOM, SICA, MERCOSUR and NAFTA. Its mission is to promote drug regulatory harmonisation for all aspects of quality, safety, and efficacy of pharmaceutical products as a contribution to the quality of life and health care of the citizens of the Member Countries of the Americas. PANDRH’s scope of harmonisation/cooperative activities includes technical guidelines, regulatory processes and the strengthening of national regulatory agencies through harmonisation of processes and standards to improve drug quality and quality assurance. Specific drug sectors covered include prescription, over the counter, generics, 'similars', biologics/vaccines and herbal medicines. 113

6.3 Promoting competition to improve availability and affordability of health products

Regional

In 2013, India implemented the Drug Price Control Order (DPCO 2013) which altered price regulation dynamics and substantially increased the number of medicines covered under price cap umbrella. DPCO 2013 allowed the National Pharmaceutical Price Policy to regulate the prices of 348 drugs covered in the 2011 Essential Drugs List. This number of drugs under price control is so much higher compared to the 74 drugs previous covered. 114 Department of Pharmaceuticals India notified the New First Schedule of DPCO, 2013 based on National list of Essential Medicines (2015) on March 10, 2016. NPPA has started the exercise of fixing the ceiling prices of the medicines in the NLEM-2015 and in a short span fixed and notified the ceiling price of 330 formulations as on June 10, 2016. The NLEM 2015 contains a total of 799 formulations under 30 therapeutic groups. NPPA is working to fix the price of these drugs as soon as possible. As on date, 969 scheduled formulations are under direct price control. 115

In Indonesia, generic pharmaceutical pricing is regulated by the government. Pharmaceuticals included in the Essential Drugs List -- 92% of which are generic and 2.5% of which are innovator -- cannot be sold for more than a 50% margin. Other generics are also subject to pricing restrictions. 115

During the country presentations in the regional meeting on GSPA-PHI assessment held in Bangkok on December 2014, Sri Lanka indicated that in order to improve local pharmaceutical production, the state offers a buy-back guarantee as well as tax incentives for investment in production. 105
Global

In 2009, the governments of Italy, the UK, Canada, Russia, and Norway as well as the Bill and Melinda Gates Foundation launched an advanced market commitment (AMC) administered by the GAVI Alliance to drive development and production of a pneumococcal vaccine specifically tailored to the needs of developing countries. The result of this innovative financing scheme suggests that AMC has been successful because:

- It has created competition – 4 suppliers have registered to sell their vaccines through the AMC at a fixed price
- It has reduced prices – suppliers have committed to selling their vaccines through the AMC at a price that is lower than $10 compared to the next lowest price on the market, and $90 less compared to the industrial market
- It has facilitated widespread demand – 30 developing countries have expressed interest in purchasing the pneumococcal vaccine through the AMC; and
- It has spurred scale-up of production capacity – the volume of the pneumococcal vaccine launch has been much higher than for any global health product historically, indicating that suppliers have scaled-up production capacity significantly

In the same year, GSK promised to cap the price of drugs in the poorest 50 nations to no more than 25% of the cost of drugs in wealthy nations. Included drugs are malaria, tuberculosis, and hepatitis. Drugs for HIV were also included, to the extent that they were not already offered at this rate. GSK also promised to invest 20% of profits made in least developed countries to build health care infrastructure in such countries.

Building on this perspective, GSK in March 2016 announced it is evolving its graduated approach to filing and enforcing patents so that IP protection reflects a country’s economic maturity. For Least Developed Countries (LDCs) and Low Income Countries (LICs), GSK will not file patents for its medicines, so as to give clarity and confidence to generic companies seeking to manufacture and supply generic versions of GSK medicines in those countries. For Lower Middle Income Countries (LMICs) generally, GSK will file for patents but will seek to offer and agree licenses to allow supplies of generic versions of its medicines for 10 years. GSK intends to seek a small royalty on sales in those countries. This offer will apply even for those countries that move out of LMIC status due to increased economic growth during this period. For High Income Countries, Upper Middle Income Countries and G20 countries, GSK will continue to seek full patent protection. Any GSK medicines on the WHO’s list of essential medicines will be included in these changes.
7 Promoting sustainable financing mechanisms

7.1 Endeavoring to secure adequate and sustainable financing for research and development

Regional

The International Finance Corporation (IFC) of the World Bank in the past 5 years has granted several loans to pharmaceutical companies in developing countries in the past 5 years, in order to increase their production and R&D capacities. Among the recent projects granted loans by IFC, 4 are from SEAR, all of which are based in India. These are:

- Bharat Biotech located in Hyderabad, India. The company is involved in the development and production of vaccines, contract development and manufacturing for developed country pharmaceutical/biotechnical companies, and development of its own line of molecules. Dabur Pharma, which is involved in marketing oncology formulations and APIs.
- Dishman Pharmaceuticals and Chemicals Limited, an Indian contract research and manufacturing company. In 2009, it began an investment program with IFC which includes construction of new facilities, establishment of a Greenfield manufacturing facility in China, and investments in overseas subsidiaries and joint ventures.
- Ocimum Biosolutions which provides contract resource outsourcing services. It is a comprehensive Integrated Life Science Informatics solutions provider with service offerings that span Sample and Data Management, Genomics Data Analysis Services such as Gene Expression, Genotyping, and Next Gen Sequencing, Bioinformatics and Genomics Databases and Bio-IT consulting services. Majority of the top 25 pharmaceutical companies, leading research institutes and emerging biotech companies worldwide have chosen it as their preferred vendor and outsourcing partner and utilize our expertise.

During the December 2014 regional meeting on GSPA-PHI assessment in Bangkok, Bangladesh reported that in the area of R&D funding, the country invests less than 1% of total health budget with top pharma investing only 0.3-0.5% of their revenues. Mid-level modern pharmaceutical companies allocate less than 0.1-0.2% of the turnover in their product development annually.

In Sri Lanka, funding for health R&D come from various sources, both national and international. Government funding comes from the National Research council; the National Science Foundation; the University Grants Commission; and the National Health Research Council. For 2015, the total research grants coming from all sectors is approximately 5 million USD.

In the same meeting, India reported that the country’s Technology Development Board under the Department of Science and Technology has provided a total funding assistance of $158.13 millions since its inception in 1996. For the health and medical sectors in particular, it has provided the following assistance:
- No. of agreements : 62
- Total cost : $128.08 million
• TDB sanction: $40.44 million

Major projects funded:

- Vaccines: Shanvac-B; Revac-B; LARV; FMD Vaccine
- Drugs: INF alfa; Indikinase; Cefixine, Betacarotene; Human growth Factor, anti-infectives
- Devices: Bone grafts; Membrane oxygenators; microarray chips; telemedicine solutions
- Facilities for: Vaccine manufacturing; API manufacturing; Organ transplant; CRO& Testing; Tissue based product development for clinical use

Global

The technical consultation meetings on innovative models for new antibiotic development held in Geneva in 2014 and the earlier workshop held in Uppsala Sweden in 2010, as described in section 4.3, are examples of expert working groups trying to examine current financing and coordination for health research and development.

While product development partnerships (PDPs) have revitalized the search for drugs, vaccines and other health technologies for the developing world, it is anticipated that they will need more funding in the coming years for expensive late-stage clinical trials as well as for expanded discovery research to replenish their product pipelines. In relation to these needs, current financing for the PDPs can be considered as too short-term, insecure and inflexible. In mid-2008, the 3 leading vaccine PDPs – Aeras Global TB Vaccine Foundation, the International AIDS Vaccine Initiative and Malaria Vaccine Initiative set-up a technical working group to explore innovative ways to finance the 3 PDPs. This group decided to analyze in greater depth the idea of augmenting grants to the PDPs with government-backed bond financing. They proposed the establishment of the PDP Financing Facility (PDPFP) whose objective is to make available, through government guaranteed loans, some of the economic and social value that their work will create in the future. Proceeds from the sale of bonds in private capital markets would be used to support R&D and then repaid when vaccines developed by the 3 PDPs came to market. The funds to repay bonds would derive from a combination of royalties on sales in high and middle-income countries and donor-funded premiums linked to sales of vaccines in low-income countries.

Another organization involved in funding health research and development is CIHR. In the early 2000s, CIHR announced that global health research was one of its five major pillars and the Global Health Research Initiative was established. It had limited funding early on, with CIHR, allocating C$29.8 million to study Neglected Tropical Diseases from 1999 to 2009. However, since 2008, there has been stronger focus in this area, and more resources were allocated in collaboration with Grand Challenges Canada. Agreements to allocate about $150 million were signed which leveraged more than double the amount of co-funding.
7.2 Facilitating the maximum use of existing financing

Regional

Most of the regional initiatives mentioned earlier in relation to technology transfer (Sections 3.4.3.1 and 3.4.2.1) are also examples of various forms of financial support provided to public-private and product development partnerships.

During the December 2014 regional meeting on GSPA-PHI assessment, India presented several models they have implemented on resource sharing and collaboration for health research and development. They have successfully implemented several inter-agency joint initiatives, examples of which are:

• Joint venture of DBT, ICMR, MoHFW with ICMR leading the initiative: “Indigenous Diagnostic technologies of TB and MDR/XDR TB developed by Indian Scientists / Companies

• CRDF Global, in partnership with the National Institute of Allergy and Infectious Diseases (NIAID), DBT, ICMR and the NIH Office of AIDS research (OAR) also funds joint teams of U.S. and Indian scientists working in tuberculosis research

• DBT – ICMR – DST Programme in Biomedical and Health Research

• CONRAD initiated DBT-ICMR joint programme on microbicides

• DBT-ICMR –IAVI initiative on HIV/AIDS

The country has also been successful in financing major innovations through PPP. A listing of such programmes is shown in Table 4 below.

Table 4. Programs funded through the PPP scheme in India and corresponding agencies involved

<table>
<thead>
<tr>
<th>AGENCY</th>
<th>PPP SCHEME</th>
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<tbody>
<tr>
<td>Department of Scientific and Industrial Research</td>
<td>Start-ups and MSMEEs scheme (PRISM)</td>
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<tr>
<td></td>
<td>Building Industrial R&amp;D promotion Program (BIRD)</td>
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<tr>
<td></td>
<td>Patent acquisition and collaborative research and technology development (PACE) scheme</td>
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<td></td>
<td>Technology development and demonstration program (TDDP)</td>
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<tr>
<td>Department of Science and Technology</td>
<td>Drug and Pharmaceuticals Research Program</td>
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<tr>
<td>National Innovation Council</td>
<td>Technology Development Board</td>
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<tr>
<td></td>
<td>Cluster Innovation Centers</td>
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<tr>
<td>Department of Information Technology</td>
<td>India Inclusive Innovation Fund</td>
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<td></td>
<td>Multiplier Grant Scheme</td>
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Part 3 of the 2012 CEWG Report by the Secretariat presented a comprehensive description of existing financial mechanisms for health R&D in various areas, and provided options on how to approach the increase of R&D funding related to Type II and III diseases and the specific needs to developing countries in relation to type I diseases. The options are either to establish a new financing mechanism or to use an existing vehicle. It also identified a number of factors which are critical for the success of any new financing mechanism which are:

- Political commitment for the establishment of the mechanisms and its mission
- An inclusive governance which represents the interests of the various stakeholders
- A broad, stable and predictable financial basis and a financial structure that minimizes procedural obstacles for contributors;
- A clearly defined, focused and realistic objective of the mechanism and a clear implementation model; and
- An effective system of monitoring the disbursement of funds and evaluation of success

A follow-up to the 2012 Report of the Secretariat is Draft Working Paper 3 on Financing Mechanisms for health R&D circulated in May 2013. The paper identified a number of mechanisms that could be suitable starting points and presents possible criteria that could be used to assess the suitability of a range of existing mechanisms. The criteria presented are more detailed that the one earlier developed by the Secretariat and includes the following items:

- Adaptability
- Scope of research in terms of 1) disease areas covered; and 2) technologies covered
- Geographical scope
- Governance
- Experience in funding R&D
- Experience if managing R&D; and
- Transparency

Twelve existing financing mechanism for health R&D were identified (ANDI; DNDI; EMBL; GAVI Alliance; Global Fund; IARC; IVI; MMV; PATH; RBM; WHO/TDR; and UNITAID) and assessed using the proposed criteria. Results were color-coded reflecting varying degrees of meeting the criteria.
with green indicating that the criterion has been fulfilled and red indicating that it is not fulfilled. WHO/TDR and the Global Fund fully satisfied the highest number of criteria at 3 each.

In June 2014, a meeting on Sustainable Investment in Research for Health was held in Berlin, Germany by COHRED, in partnership with the West African Health Organization (WAHO) and NEPAD. The meeting had 4 key discussion topics, namely: developing an integrated system for innovation; shifting from the notion of “funding” to “investment”; creating an African research space; and engaging in advocacy for research for health financing. Some of the major recommendations arrived at during the meeting corresponding to each discussion topic are shown below.

Table 5. Major recommendations given during meeting on Sustainable Investment in Research for Health: Berlin, Germany June 2014

<table>
<thead>
<tr>
<th>Developing an integrated system for innovation</th>
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<tbody>
<tr>
<td>Make an economic case for research by linking research to cost-effectiveness and return-on-investment studies</td>
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<tr>
<td>Show the actual investments made in research to demonstrate tangible return on investment</td>
</tr>
<tr>
<td>Increase cross-sectoral research collaboration to make research more efficient and sustainable</td>
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<table>
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<th>Shifting from a funding to an investment perspective</th>
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<tbody>
<tr>
<td>Show the impact of research on GDP to demonstrate the economic value of research in its own right</td>
</tr>
<tr>
<td>Track research through open data systems to show impact and return on investment</td>
</tr>
<tr>
<td>Create integrated research and innovation platforms to make efficient use of existing resources and thereby incentive investments</td>
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<table>
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<tr>
<th>Creating an African research space</th>
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<tr>
<td>Harmonize stewardship through tapping into regional leadership bodies and establishing common regulation processes and research agendas</td>
</tr>
<tr>
<td>Engage all stakeholders through open dialogue and continuous feedback, both during the creation of this space and its operation</td>
</tr>
<tr>
<td>Secure consistent funding by identifying a range of funding mechanism to ensure sustainability of the research space</td>
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<table>
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<tr>
<th>Engaging in advocacy</th>
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<tr>
<td>Establish a regional peer-review mechanism to incentivize follow-up of key declarations, using a defined set of indicators</td>
</tr>
<tr>
<td>Engage the media as an advocate by maximizing opportunities to communicate research findings through research-savvy journalists and media-savvy researchers</td>
</tr>
<tr>
<td>Widen the scope of the audience to include for example, other ministries and stakeholders</td>
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The same meeting report presents, as an Appendix, a comprehensive and detailed listing of innovative financing mechanism for health R&D including those which are already currently operational, as well as those which are still in the proposal stage. The listing was put-together by combining information derived from the work of three groups who have made in-depth studies of various funding mechanisms, namely:

1. CEWG which provided, as part of its 2012 report, a review of innovative financing proposals, and assessed these based on a number of pre-determined criteria;  

2. Michaud and Kates who outlined a classification system of the different types of innovative financing mechanism for global health and provided an inventory of those that are either proposed or currently being used. This work was commissioned by the Henry J. Kaiser Family Foundation in 2011 to identify how the US government can or should participate in such mechanisms; and

3. The Milken Institute who convened a Financial Innovations Lab in 2012 to map current and potential innovative financing models with the goal of leveraging traditional sources of aid to attract private-sector investment and increase sustainable funding for R&D.

8. ESTABLISHING MONITORING AND REPORTING SYSTEMS

Monitoring and evaluation is an integral component of the WHO strategy on research for health. In order to monitor the implementation of the elements and their impact a framework has been developed, under which, the elements of the strategy were organized using the “logic model” of inputs/activities, outputs, outcomes and impacts, and corresponding indicators were defined. 

The development of the framework and methodologies for assessment of national health research systems in general started in 2001 by COHRED. The COHRED assessment methodology has been extensively applied covering several countries all over the world, including SEARO-member countries. A M&E framework for GSPA-PHI was formulated during 2011 discussion focused solely on element 8 of GSPA.

8.1 Measuring performance and progress towards objectives contained in the strategy and plan of action

Element 8 of the GSPA calls for the establishment of systems to monitor performance and progress of the implementation of each element, particularly on the following areas:

a. Gaps and needs related to health products and medical devices in developed and developing countries;

b. Impact of intellectual property and other issues addressed in the CIPIH report on the development of, and access to health care products from a public health perspective;
c. Impact of incentive mechanisms on innovation of and access to health products and medical devices; and
d. Investment in research and development to address the health needs of developing countries

During the sixty-second World Health Assembly Meeting in 2009, a set of 30 progress indicators were presented to the Executive Board, which would form the basis for regular reporting to the Health Assembly on performance and over-all progress made over a 2-year reporting period, as well as inform the evaluation of the strategy at the end of four years. The indicators covered all the 8 GSPA elements and were applicable to both research-based health pharmaceutical products and traditional medicines.\textsuperscript{132}

**Regional**

Sri Lanka is the only SEAR country to carry out GSPA-PHI assessment, i.\textsuperscript{133} The findings showed the existence of several R&D focused institutions, and there is a need for co-ordination, among them to achieve better results.

Other countries like Thailand and Indonesia have performed evaluation under COHRED guidance and India is part of EVAL-HEALTH\textsuperscript{135}.

**Global**

It was reported during the Sixty-seventh World Health Assembly held in March 2014, that the Secretariat, in collaboration with the Regional Office for the Americas, is developing the Global Platform on Innovation and Access which is an online portal for monitoring the progress made by Member States and other stakeholders in implementing the GSPA-PHI. The platform will be comprised of an information hub, a knowledge repository and a virtual forum on innovation. It was scheduled to be launched in April 2014.\textsuperscript{137}

In Africa, a pilot monitoring tool to monitor the implementation of GSPA-PHI was developed in 2009 by IQSensato and Health Action International (HAI) Africa. The tool was piloted in Ghana, Uganda, Zimbabwe, Rwanda and Kenya. It is composed of a questionnaire to be accomplished by stakeholders in the R&D process (ex., officers from the Ministry of Health, the academe, Medical Research Institutes, Intellectual Property Offices, etc.). The pilot phase highlighted the need to prepare a short guide for the questionnaire which forms the basis for data collection.\textsuperscript{138}

While the systematic and institutionalized monitoring and evaluation of GSPA-PHI can still be considered as work in progress, several major initiatives have long been developed and implemented to monitor and evaluate specific areas related to health research and development. For example, in the area of health research capacity strengthening, a planning, monitoring and evaluation framework has been developed and implemented by the TDR-based ESSENCE (Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts) on Health Research. This project is an initiative between funding agencies to scale-up coordination and harmonization of research capacity investments.\textsuperscript{139}
It is in the area of monitoring financial flows in support of health research and development where several initiatives by other international organizations have been implemented. During a WHO informal workshop on this topic held in London in February 2013, the following health-focused initiatives were presented, among others.

a. G-Finder – This initiative is part of Policy Cures and has been funded by the Bill and Melissa Gates Foundation since 2008. They measure funding on 31 neglected diseases which were identified using a panel of international experts, predominantly focusing on diseases which disproportionately affect low and middle-income countries.

b. Health Research Web (HRWeb) – It provides an online platform to upload as well as share information on R&D initiatives, policies and strategies. It aims to provide practical information and includes publications and analysis of health systems. The HRWeb model has allowed the development and publication in different forms of media, analysis about national health research systems in Latin America, and has engaged delegates from the science, technology and health sectors in the Latin American Conferences on Research and Innovation for Health (www.paho.org/LACRIH).

c. World RePORT – World RePORT (http://worldreport.nih.gov) is seen as a public tool to track funding and activities so one can analyze the complete landscape of research funding, identify funding gaps and areas where there may be a duplication of efforts, seek problems where collaboration would be useful, and improve efforts to work more effectively and synergize investments in research. The inter-active database provides descriptors of the research collaborations and funding by all NIH Institutes and Centers and its 8 affiliated organizations with institutions in sub-Saharan Africa.

Since a number of indicators needed to monitor and evaluate the progress of GSPA implementation cannot be derived from routinely collected data, there is a need to conduct special studies to develop study designs and data collection methodologies to address this need. Like the method developed by WHO, Viergever to identify gaps in health R&D.
9. GSPA elements and way forward: some suggestions

This section presents some suggestions for the next steps to be taken with respect to each of the elements of the GSPA-PHI. The suggestions are culled from recommendations given in some of the literature reviewed. However, this section is still a work in progress since its final version will incorporate the inputs of Member States and research institutions to the questionnaire on Regional Situational Analysis which was sent to the workshop participants to be accomplished prior to the workshop.

1. Prioritizing research and development needs

- In the area of local production of medicines, a primary objective must be to identify therapeutic areas and regions for which existing production does not meet local needs, including needs for long-term sustainable supply. Objectives of the work programme/action plans to be developed should be designed to address those unmet needs.

- Further research is required in two areas:
  a. Measuring private sector technology transfer flows; and
  b. Understanding the conditions under which local production leads to improved access to medicines, and the pathways through which such improvements occur

2. Promoting research and development

International partnerships that provide technical assistance and access to technology should be expanded. Although bilateral partnerships like that of PATH and the Bharat rotavirus project in India have been very useful, access to some technologies could be shared on a more open, multi-lateral basis. One such model is the WHO “technology hub” for influenza vaccines which made production know-how available to developing country manufacturers.

3. Building and improving innovative capacity

- Research organizations should engage with country leadership and other stakeholders to assess the adequacy of current national research capacity and use the assessment results as inputs in determining the most effective role they can play to support the development of research capacity that addresses the health and development needs of the country.

- Advocate for the development of policies on retention and career development of human resources for health research
• Expand opportunities for production staff of local drug manufacturers to include practical training which would complement the theoretical training provided by academic institutions. Such type of training is amenable to both north-south and south-south cooperation, since several developing countries are no home to advanced industries that could provide training opportunities to nationals of developing countries.

• WHO technical experts can work with private-sector companies to design and make available “modular packages” for local production facilities suited for developing countries, including advanced formulation facilities. WHO can work with the World Bank to design a financing package for such facilities.

4. Transfer of technology

• Better, stronger and wider dissemination of needs and required procedures -- International health donors and government agencies should send clearer signals to product developers about the products they wish to buy, the technical standards that have to be met, and approval and procurement procedures which need to be followed. This is particularly true for diagnostics where product needs and assessment procedures have not been properly well defined at different levels.

• Capacity building on how to negotiate effective technology transfer agreements may be useful, particularly for firms with limited experience in this area.

5. Application and management of intellectual property to contribute to innovation and promote public health

• Ongoing efforts in training national drug regulatory authorities and policy makers on how to implement TRIPS in a manner that protects public health and expands the space for local production should be strongly supported and continued.

6. Improving delivery and access

• Countries need to streamline their system for regulating pharmaceutical and biotechnology R&D needs, and strengthen their systems and capacity for evaluating new technologies. At the same time, international systems for assessing and recommending products, especially WHO’s prequalification program for diagnostics need to be expanded so they can handle more products more rapidly.
WHO should continue to work with national and regional regulatory authorities to coordinate and further integrate rules and mechanisms for approving and monitoring operation of pharmaceutical production facilities.

7. Promoting and sustaining financing mechanisms

- Both the government of Member States and international donors should expand financing for promising neglected disease product development projects, including for late-stage clinical trials and for new innovation-driven firms. Joint financing schemes like the existing collaboration between the Department of Biotechnology of India and the Wellcome Trust are a promising way to channel international funding for health R&D

8. Establishing monitoring and reporting systems

- There is a need for improved information about ongoing initiatives to provide a stronger evidence base for policy analysis and recommendations. A methodical, comprehensive, regularly updated and publicly accessible database of relevant initiatives is currently lacking but is badly needed in the current fragmented landscape.

- Start activities for the development of the Regional Health Observatory in a phased way in 3 steps, as recommended by the 2012 Report to the Secretariat, as follows: 1) research phase; 2) planning phase; and 3) pilot-testing phase. The Region should already start the research phase (needs assessment and situational analysis) for this undertaking.

- The current tool available for the assessment of GSPA-PHI progress is relatively complicated and difficult to implement. There is a need to make the tool more user-friendly to encourage more countries to use it. The experience of countries like Sri Lanka who have used the tool will be very useful inputs in simplifying it.
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### Annex 1

**BOX 1: WHA RESOLUTIONS, WORKING GROUPS ESTABLISHED AND MEETINGS CONDUCTED RELATED TO INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH**

<table>
<thead>
<tr>
<th>RESOLUTIONS/ WORKING GROUPS/ MEETINGS</th>
<th>IMPORTANT RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Resolution WHA56.27 (Intellectual Property Rights, Innovation and Public Health) adopted by the 56th World Health Assembly; May 2003</td>
<td>1.1 “....to establish the terms of reference for an appropriate time-limited body to collect data and proposals from the different actors involved and produce an analysis of intellectual property rights, innovation and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries.”¹</td>
</tr>
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<td></td>
<td>1.2 Publication of the CIPIH Report in 2006</td>
</tr>
<tr>
<td>1.1 Establishment of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) in 2004</td>
<td></td>
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<tr>
<td>1.2 Recommendation 6.1 of the CIPIH Report:</td>
<td>“WHO should develop a Global Plan of Action to secure enhanced and sustainable funding for developing and making accessible products to address diseases that disproportionately affect developing countries.”²</td>
</tr>
<tr>
<td>2.1 Resolution WHA59.24 (Public Health, Innovation, Essential Health Research and Intellectual Property Rights: Towards a Global Strategy and Plan of Action) adopted by the 59th World Health Assembly: May 2006</td>
<td>To establish an intergovernmental working group (IGWG) to “draw-up a Global Strategy and Plan of Action in order to provide a medium-term framework based on the recommendation of the Commission”. Such a strategy and plan of action would aim at (a) securing an enhanced and sustainable basis for needs-driven, essential health research and development relevant to diseases that disproportionately affect developing countries; (b) proposing clear objectives and priorities for research and development; and (c) estimating funding needs in this area”.³</td>
</tr>
<tr>
<td>2.2 Establishment of the Inter-governmental Working Group on Public Health, Innovation and Intellectual Property (IGWG) which met from Dec. 2006 to May 2008</td>
<td></td>
</tr>
<tr>
<td>3. Resolution WHA 59.26 (International Trade and Health) adopted by the 59th World Health Assembly on May 2006</td>
<td>Called upon WHO to provide assistance to Member States to frame coherent policies to address the relationship between trade and health; to respond to Member States’ requests for support in their efforts to build the capacity to understand the implications of international trade and trade agreements for health; and to address relevant issues through policies and legislation.⁴</td>
</tr>
<tr>
<td>4. Resolution WHA 60.30 (Public Health, Innovation and Intellectual Property)</td>
<td>The WHO Director General was requested, amongst others, to:⁵</td>
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</table>
### BOX 1: WHA RESOLUTIONS, WORKING GROUPS ESTABLISHED AND MEETINGS CONDUCTED RELATED TO INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH

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<tr>
<td>adopted by the 60th World Health Assembly on May 2007</td>
<td>1. provide technical and financial support for regional consultative meetings in order to set regional priorities that will inform the work of the Intergovernmental Working Group; and 2. encourage the development of proposals for health-needs driven research and development for discussion at the Intergovernmental Working Group that includes a range of incentive mechanisms including also addressing the linkage between the cost of research and development and the price of medicines, vaccines, diagnostic kits and other health-care products and a method for tailoring the optimal mix of incentives to a particular condition or product, with the objective of addressing diseases that disproportionately affect developing countries;</td>
</tr>
<tr>
<td>5.1 Resolution WHA61.21 (Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property) adopted by the 61st World Health Assembly: May 2008</td>
<td>Global Strategy and Plan of Action has 8 elements, of which the 7th element covers promoting sustainable financing mechanisms. Among the key actions to be taken is to “establish a result-oriented and time-limited expert working group under the auspices of WHO and linking up with other relevant groups to examine current financing and coordination of research and development, as well as proposals for new and innovative sources of financing to stimulate R&amp;D related to Type II and Type II diseases and the specific R&amp;D needs of developing countries in relation to Type I diseases”.</td>
</tr>
<tr>
<td>5.2 Establishment of the Expert Working Group on Research and Development: Financing and Coordination in November 2008. This EWG on R&amp;D submitted its Final Report to the 63rd WHA in 2010</td>
<td></td>
</tr>
<tr>
<td>6. Resolution WHA62.16 (Global strategy and plan of action on public health, innovation and intellectual property) adopted by the 62nd World Health Assembly: May 2009</td>
<td>The Director-General was requested to: 1. significantly increase support towards greater efficiency and effectiveness in the implementation of the global strategy and plan of action on public health, innovation and intellectual property and prioritize concrete actions in the area of capacity-building and access; and 2. in addition to continued monitoring, to conduct an overall programme review of the global strategy and plan of action in 2014 on its achievement, remaining challenges and recommendations on the way forward to the Assembly in 2015 through the Executive Board.</td>
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</table>
## BOX 1: WHA RESOLUTIONS, WORKING GROUPS ESTABLISHED AND MEETINGS CONDUCTED RELATED TO INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH

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<tr>
<td>7.1 Resolution WHA63.28 (Establishment of a Consultative Expert Working Group on Research and Development: Financing and Coordination) adopted by the 63rd World Health Assembly: May 2010.</td>
<td>“...to establish a Consultative Expert Working Group that shall: (a) take forward the work of the Expert Working Group; (b) deepen the analysis of the proposals in the Expert Working Group’s report”</td>
</tr>
<tr>
<td>7.2 Establishment of the CEWG in 2010. Final Report entitled “Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination” was submitted to the 65th WHA in May 2012</td>
<td>—</td>
</tr>
<tr>
<td>8. Resolution WHA65.22 (Follow up of the Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination) adopted by the 65th WHA: May 2012</td>
<td>a. Urged member States “to hold national level consultations among all relevant stakeholders in order to discuss the CEWG report and other relevant analyses, resulting in concrete proposals and actions”.</td>
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<td></td>
<td>b. Requested the Director General “to hold an open-ended meeting of member States that would thoroughly analyse the report and the feasibility of the recommendations proposed by the Consultative Expert Working Group, and taking into account discussion during regional committee meetings and regional and national consultations”.</td>
</tr>
<tr>
<td>9. Conduct of the Open-ended meeting of Member States on the follow-up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination in Geneva on 26-28 November 2012.</td>
<td>• Chaired by Dr. Viroj Tangcharoensathien of Thailand</td>
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<td>• SEA/RC65/R3 used as working draft in the formulation of draft resolution adopted during this meeting</td>
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<tr>
<td>RESOLUTIONS/ WORKING GROUPS/ MEETINGS</td>
<td>IMPORTANT RECOMMENDATIONS</td>
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| 10. Resolution WHA66.22 (Follow-up of the Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination) adopted by the 66th World Health Assembly: May 2013 | Requested the Director General to:  
  a. develop norms and standards for classification of health research and development, building on existing sources, in consultation with Member States and relevant stakeholders, in order to collect and collate information systematically  
  b. facilitate through regional consultations and broad engagement of relevant stakeholders the implementation of a few health research and development demonstration projects to address identified gaps that disproportionately affect developing countries, particularly the poor, and for which immediate action can be taken |
**Annex 2**

### BOX 2: ACTIVITIES RELATED TO CEWG RECOMMENDATIONS CONDUCTED AT THE REGIONAL LEVEL

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>IMPORTANT RECOMMENDATION/OUTCOME</th>
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<tbody>
<tr>
<td>1. Conduct of Regional Consultation for <em>Development of a Regional Framework on Public Health, Innovation and Intellectual Property</em> in New Delhi on 5-6 April, 2011</td>
<td>SEAR Member States identified national and regional priorities for the 8 elements and 25 sub-elements of the GSPA, and presented a set of recommendations for WHO and Member States of the region that requires further engagement at national, regional and global levels.</td>
</tr>
<tr>
<td>2.1 Conduct of Regional Technical Consultation in Bangkok, Thailand on 15-17 August 2012</td>
<td>“To engage actively in the negotiations in an open-ended meeting of Member States in November 2012, inter alia, by supporting the development of the Global Health R&amp;D Observatory, effective global R&amp;D coordination, adequate and sustainable funding for R&amp;D on diseases of Type II and III and specific R&amp;D needs of diseases of Type I in developing countries.”</td>
</tr>
<tr>
<td>2.2 Regional technical discussion of the CEWG Report conducted during the 65th SEA Regional Committee Meeting in Yogyakarta, Indonesia on 7 Sept. 2012</td>
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<tr>
<td>2.3 Regional Resolution SEA/RC65/R3 (Consultative Expert Working Group on Research and Development: Financing and Coordination) adopted during 65th SEA Regional Committee Meeting</td>
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<tr>
<td>3.1 Conduct of country studies in Thailand, India, Bangladesh, Sri Lanka and Indonesia to document existing norms and standards followed in the classification of health R&amp;D activities; to identify current and future priorities for R&amp;D for health products and to identify project which need to be implemented in order to develop and deliver priority health products</td>
<td>The participants of the Regional Consultation presented 6 recommendations for the development of norms and standards for the classification of health R&amp;D towards setting-up of R&amp;D observatories. These include, among others, the following:</td>
</tr>
<tr>
<td>3.2 Conduct of Regional Consultation for <em>Developing a Strategic Workplan as a follow-up of the Report of the Consultative Expert Working group (CEWG) on Research and Development: Financing and Coordination</em> held in Bangkok, Thailand on 25-26 July 2013</td>
<td>a. Setting-up of a national R&amp;D observatory to collect, analyse, coordinate, prioritize and monitor R&amp;D resource flows from the public and private sectors;</td>
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<td>b. Member States may develop modalities and identify institutional entities to develop, establish, maintain and manage health R&amp;D observatories;</td>
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<td>c. Member States may pilot-test the proposed classification grid for norms and standards for R&amp;D in terms of diseases, product development and policy.</td>
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<td>In the same meeting, 7 potential priority areas for R&amp;D demonstration projects were identified and ranked.</td>
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<tr>
<td>ACTIVITY</td>
<td>IMPORTANT RECOMMENDATION/OUTCOME</td>
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</table>
| 4. Meeting of Experts on Demonstration Projects held in New Delhi, India on 24-25 October 2013 | Identified 4 research and development demonstration projects for submission to and consideration at the Technical Consultative Meeting to be held in Geneva on 3-5 December 2013. These were:  
   1. Combatting tuberculosis in the region (development of diagnostics and drugs)  
   2. Project on medicines and devices for diabetes mellitus  
   3. Multiplexed point-of-care test for acute febrile illness  
   4. Dengue vaccine development |
| 5. Regional Meeting for the Assessment of Progress in Implementing Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property for Southeast Asia held in Bangkok, Thailand on 16-18 December, 2014 | Member States agreed to provide a self-assessment as established by WHA62.16 and develop a priority mapping for the GSPA next steps, using the matrix agreed upon during the Consultation. WHO is asked to summarize and consolidate the results of the GSPA self-assessment and forward it from SEARO to WHA.  
Specific actions by Member States and WHO in relation to each of the 8 GSPA elements were also identified. |
<table>
<thead>
<tr>
<th>Country</th>
<th>Activities</th>
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</table>
| Bangladesh | - Identification of research priorities in Bangladesh falls under the purview of the Bangladesh Medical Research Council (BMRC, a national organization under the Ministry of Health & Family Welfare (MOH&FW).
- In 2011, WHO SEARO requested the Bangladesh to examine the “National R&D priorities for Bangladesh and identify priority demonstration projects based on the local pharmaceutical manufacturing industry’s needs for improved technology and their capabilities for technology absorption, as per road map suggested by the Consultative Expert Working Group (CEWG) on Research and Development
- The following priority innovative projects were identified:
  a. Phytochemical profiling, standardization and quality control of traditional and herbal drugs to ensure their safety and efficacy;
  b. Discovery of the new chemical entities from medicinal plants, microbes and marine sources.
  c. Process Development and Validation to Synthesize Active Pharmaceutical Ingredients (APIs): Laboratory Scale to Industrial Scale through Pilot Scale production of bulk drugs.
  d. Production of high value biopharmaceuticals/catalysts by recombinant DNA technology and fermentation technology. |
| Bhutan | - Initiated a process for research priority setting in November 2014 where a workshop was held and a report is yet to be published |
| India | - Priority setting in India is done based on the following:
  o Global Forum for Health Research (GFHR), ACHR framework
  o WHO SEARO- Regional Priorities
  o The WHO-India Country Cooperation Strategy (CCS) 2012-2017
  o National Institute of Health- Global Priority |
| Indonesia | - The National Research Agenda 2010-2014 covered the development of vaccines, drugs of raw materials, traditional medicines, health and medical devices, etc.
- The National Research Agenda 2015-2019 on health sector is going to be finalised based on burden of disease
- MoH Decree no.87/2013 provides road map on drugs raw materials development |
| Myanmar | - National Health Policy of Myanmar has a policy guidance to encourage conduct of medical research activities not only on prevailing health problems but also giving due attention to health system research.
- Promotion of Health Research should be done with the objective of conducting health researches that will contribute to health sector development |
### BOX 3. PRIORITY-SETTING ACTIVITIES OF SEAR MEMBER STATES ON HEALTH RESEARCH AND DEVELOPMENT

<table>
<thead>
<tr>
<th>Country</th>
<th>Priority actions include conducting research in the following areas:</th>
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<tbody>
<tr>
<td></td>
<td>• Health policy and Health system</td>
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<td>• Communicable diseases</td>
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<td>• NCDs</td>
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<td></td>
<td>• Environmental health</td>
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<td></td>
<td>• Traditional medicine</td>
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<td></td>
<td>• Academic and technology development</td>
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<td></td>
<td>• Capacity strengthening</td>
</tr>
</tbody>
</table>

**Nepal**
- The following areas have been identified as priority research areas under NHP 2014: National data collection systems on access to service / medicines, service standards, disease burden, NCD prevalence, ppp in basic health service delivery, coordination between utiliser and producers of HRH, HI, investment on health, equality and equity, community participation, VfM, regulation, TRM research, incentive, sharing of res finding

**Sri Lanka**
- Priority setting for health research is done by the National Health Research Council (NHRC)
- The National Research and Development Investment Framework for Sri Lanka 2015-2020 has an investment plan amounting to LKR 50 billion covering 10 sectors including health

**Thailand**
- Thailand’s national plan and strategy on innovation has the following provisions:
  - 1st 10-year plan (2012-2021): Green innovation
  - Increasing human resource in R&D to 25 per 10,000; 60% working in private sector
  - R&D investment ≥ 2% GDP; private ≥ 70%
  - Main target in health: preventable diseases and emerging diseases with domestic science, technology and innovation in order to reducing imported technology
- R&D projects in the pipeline includes:
  - Vaccines: enterovirus, flu, dengue (research and development)
  - Medicines: HIV/AIDS (development)
  - Diagnostics: Melioidosis
  - Medical devices
### BOX 4. NATIONAL COORDINATING BODIES FOR HEALTH RESEARCH AND DEVELOPMENT IN THE SEAR MEMBER STATES

<table>
<thead>
<tr>
<th>Country</th>
<th>Coordinating Body for Health Research and Development</th>
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</table>
| **Bangladesh** | • **Bangladesh Medical Research Council (BMRC)** is a research coordinating organization which serves as the focal point for health research in the country. Its main activities include the promotion & coordination of health research, funding research studies, research capacity strengthening & utilization of research results. It has members representing post-graduate medical institutes, medical colleges, universities, learned societies including Bangladesh Association of Pharmaceutical Industries, medical institutions, health related organizations, various divisions and departments of of the ministries dealing with medical education, services and research.  
  • **The Health, Population, Nutrition Sector Development Program (HPNSDP)** has allocation on research and development for the year 2011-2016. Under the HPNSDP, the Planning Unit of the Directorate General of Health Services and the BMRC are the principal bodies for conducting & coordinating research. The following institutions have also R&D allocations:  
  o Health Economics Unit of the Ministry of Health  
  o National Institute for Population Research & Training (NIPORT)  
  o NIPSOM, IEDCR & ICDDR’B  
  • **The Program Management & Monitoring Unit (PMMU) of MoH** play a stewardship role for coordination & dissemination of key research results. |
| **Bhutan** | • Collaboration for health research and development is almost non-existent in the country, but some agencies are taking initiatives to collaborate. For example, the National Biodiversity Centre (NBC) is collaborating with international companies in Bio prospecting.  
  • Hospitals/institutes engaged in disease control/health research include the:  
  o Faculty of Nursing and Public Health under UMSB  
  o Malaria Control Program  
  o NGOs  
  o Menjong Sorig Pharmaceutical (MSP)  
  o Faculty of Nursing and Public Health under UMSB |
### BOX 4. NATIONAL COORDINATING BODIES FOR HEALTH RESEARCH AND DEVELOPMENT IN THE SEAR MEMBER STATES

<table>
<thead>
<tr>
<th>Country</th>
<th>Coordinating Body for Health Research and Development</th>
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</table>
| Indonesia | • There is no system in place to share the resources and networking  
• MoH is the coordinator for national health research (MoH Decree no.791/1999)  
• Institutes engaged in medical research include: NIHRD, the National Research Council, Indonesia Institute of Science, Ministry of Research & Technology and the universities. Hospitals are also engaged in disease control/health research and collaborate with NIHRD in doing surveillance and clinical studies  
• Various forms of collaboration in health R&D are between government institutions; between sectors; between government and private research Consortium.  
• International collaboration especially in terms of resource sharing and networking is usually between WHO and INA Respond (Indonesia Research Partnership on Infectious Diseases) |
| Maldives | • The country has no official R&D institute. Small operational researches are conducted in health facilities and in Maldives National university  
• Hospitals/institutes engaged in disease control/health research have their own Health Research Committee which takes charge of coordination and collaboration, as needed |
| Myanmar | • The MoH Department of Medical Research is responsible for health research and development. However, under each and every Department of the MoH, there are research programmes in various fields – like clinical, epidemiological, public health, HSR etc.  
• Institutes engaged in medical research include the Medical Universities, University of Public Health and other paramedical universities. Hospitals/institutes are also engaged in disease control/health research. All the central, S&R, district and township hospitals including the station hospitals provide data on disease incidence and prevalence, and conduct some researches in their area of interest.  
• Coordination and collaboration between the MOH departments and universities is the responsibility of the MoH. However, improvements are needed in the current system of resource sharing/networking. |
<p>| Nepal | • The institutes involved in health research and development in |</p>
<table>
<thead>
<tr>
<th>Country</th>
<th>Coordinating Body for Health Research and Development</th>
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<tbody>
<tr>
<td>Nepal</td>
<td>NHRC, Public sector medical colleges, VBDRC, NAST, NARC, Ayurveda Res Centre, BPKHIS, NAMS and NTP. Hospitals / institutes engaged in disease control / health research but only to a limited extent since service delivery undermines research in general. • R&amp;D collaborations is done at the program level like BPKIHS, IoM. Systems of resource sharing/networking are implemented for NHRC coordinated grants, UGC, etc.</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>• The National System for Research and Development (NSRD) is coordinated by the Coordinating Secretariat for Science, Technology and Innovation (COSTI). • Policy guidance for NSRD is provided by the National Science and Technology Commission (NASTEC). However, COSTI, NSF, and NHRC also play a role.</td>
</tr>
<tr>
<td>Thailand</td>
<td>• There are various venues for coordination and collaboration in Thailand, as follows: o Public and private: mechanism through the MoST (NSTDA) and industries; Science Park o Public to public (science and technology to other areas of science): routine forum between funding agencies and research institutes o Science and technology to medical science: target-based budget allocation between NRCT and HSRI (pilot project)</td>
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<tr>
<td>Country</td>
<td>Regulatory Body/Mechanism</td>
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| Bangladesh | • The Directorate General of Drug Administration (DGDA) is the Drug Regulatory Authority (DRA) of pharmaceutical products and vaccines in Bangladesh. The DRA is the sole authority responsible for monitoring and supervision of all activities related to import, procurement of raw materials, production and import of finished drugs, export, sale, pricing, etc. for all kinds of medicine.  
• The National Drug Policy (2005) states that the WHO’s current Good Manufacturing Practices (GMP) should be strictly followed and that manufacturing units will be regularly inspected by the DRA.  
• At present in Bangladesh there is one Central Ethics Review Committee and 9 Institutional Research Ethics Committees, attached to 9 institutions in the country.  
• The ERC of the Bangladesh Medical Research Council (BMRC) is the Central Ethics Review Committee, called the National Research Ethics Committee (NREC). BMRC serves as its Secretariat  
• BMRC Policy stipulates that each and every Project Proposal approved by the Scientific Review Committee must get ethical approval before funding.  
• The NREC provides approval for:  
  o BMRC Funded Research Projects (Internal/Intramural)  
  o Projects funded by Organizations (National and International) other than BMRC (External/Extramural), including multicentre collaborative studies.  
  o Research studies leading to Postgraduate Degrees (Specifically PhDs). |
| Bhutan     | • The Drug Regulatory Authority of Bhutan (DRA) was established under the Medicines Act of Bhutan 2003. The National Medicines Board is tasked to oversee the DRA  
• Other regulatory bodies and instruments in the country include:  
  o National Drug policy 2007  
  o EDL developed by National Drug Committee  
  o The Bhutan Medicine Rules and Regulation 2008  
  o Essential Medicine Policy for both Traditional & Allopathic medicines, EMTD  
  o Bhutan Medical and Health Council  
  o Quality Assurance and Standardization Division  
  o Research Ethics Board of Health (REBH)  
• Both traditional and allopathic medicines are coordinated by DRA but vaccines surveillance done by VPDP (AEFI)  
• There is a proposal to put in place the national antibiotics policy in collaboration with the Ministry of Agriculture and forest.  
• The National Medicines Policy of Indonesia provides for:  
  o Availability, affordability, sustainability of essentials medicines,
<table>
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<tr>
<th>Country</th>
<th>Regulatory Body/Mechanism</th>
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<tr>
<td>Maldives</td>
<td>Legal/regulatory framework is covered by medicine regulation and Consumer Protection Law</td>
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<td></td>
<td>Both the Ministry Of Health and academic institutions have established their Ethics Committees</td>
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<tr>
<td>Myanmar</td>
<td>The Nation Drug Law was enacted in 1992 to ensure access by the people safe and efficacious drugs. It describes the requirements for licensing in relation to manufacturing, storage, distribution and sale of drugs. It also includes provisions on formation and authorization of Myanmar Food and Drug Board of Authority.</td>
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<td>Traditional Drug Law (1996) - Concerned with labeling, licensing and advertisement of traditional drugs to promote traditional medicine and drugs. It also aims to enable public to consume genuine quality, safe and efficacious drugs. The law also deals with registration and control of traditional drugs and formation of Board of Authority and its functions.</td>
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<td></td>
<td>The Ethics committees are based at the DMR. There is also an ethical review committee under the DOH, but it does not have much experience in the field of clinical trials</td>
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<tr>
<td>Nepal</td>
<td>Basis for regulation is Drug Act 2078 (DDA &amp; NML)</td>
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<td>No separate rule for vaccines and biological, however DDA is adopting WHO recommended procedures to approve vaccine.</td>
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<td>Public sector NIP vaccines are allowed if they are WHO PQ.</td>
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<td>Lot release procedure is adopted prior to marketing of such products from NML</td>
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<tr>
<td></td>
<td>Ethics committees – NHRC / Ethical Review Committee</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>Regulation of pharmaceuticals and clinical trials done by the Cosmetics Devices and Drugs Regulation Authority (CDDA) established under the CDDA Act of 1980. Responsibilities of CDDA include the following:</td>
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<tr>
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<td>o Good Manufacturing Practice (GMP) inspections</td>
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<td>o Ensuring compulsory inclusion of bioequivalence data in product dossiers</td>
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<td>o Evaluation of biosimilar products according to WHO guidelines</td>
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<td>o Regulation of active pharmaceutical ingredients (API)</td>
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<td></td>
<td>o Strengthening of post-marketing surveillance</td>
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<td>o Strengthening of pharmaco-vigilance</td>
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<td>Country also has a National Medicinal Drug Policy (2006) which created the National Medicinal Drug Regulatory Authority with a Division for Clinical Trial</td>
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<td>- Ethics oversight is provided by 8 Institutional Ethics Review Committees recognized by the CDDA. The ethics review system is under the umbrella of the Forum for Ethics review Committees in Sri Lanka (FERCSL) established by the Sri Lanka Medical Association.</td>
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<td>- Registration of clinical trials is done through the Sri Lanka Clinical Trials Registry which was established and managed by the Sri Lanka Medical Association since 2006</td>
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Executive Summary

Member states of our Region requested (in High Level Preparatory Meeting for the Regional Committee, July 2014) to take up an assessment of Global Strategy and Plan of Action on public health innovation and intellectual property (GSPA) so as to inform/assist decision making in WHA in 2015. An assessment of GSPA was mandated by WHA 62 that called upon the public health community “to conduct an overall programme review of the global strategy and plan of action in 2014 on its achievement, remaining challenges and recommendations on the way forward and report to the Assembly in 2015 through the Executive Board” (WHA62.16 para 6).

The main objective was to enable development of a regional position during “Regional Meeting for Assessment of Progress in Implementing Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property for SE Asia” documents were developed to assist global strategic decision making on GSPA. The technical papers attempted to record and document experiences and identify the opportunities and challenges in operationalizing the GSPA that may inform decision making on next steps in this regard.

To contribute to the discussions on follow up GSPA (WHA61.211) five technical papers from experts relevant to the core of the Global strategy and plan of action on public health, innovation and intellectual property (GSPA-PHI) were presented at the SEAR regional meeting during 16-18 December 2014 in Bangkok for assessment of progress in implementing global strategy and plan of action on public health, innovation and intellectual property (GSPA-PHI) for South East Asia. These were:

1. The Global Platform on Innovation and Access to medical products and technologies by Ms Claudia Nannei, Technical Officer, WHO Headquarters, background paper is National Assessment Tool: To assist member states in implementing the global strategy and plan of action on public health, innovation and intellectual property.

2. R&D for Neglected Patients: Changes over the Past Decade and Future Challenges by Dr Bernard Pecoul, Executive Director, DNDi, based on the technical paper Innovation + Access: The Urgent Need for a New Paradigm for Biomedical Innovation.

3. Principles for developing collaborating networks, academia and public-private partnership engagement for research and innovation – the Africa, Asia and South America context by Simon Croft, Amino Sugimoto and Javier Lezaun.

4. For Developing a multidisciplinary approach for global health - clinical, epidemiological and basic research: A personal perspective by Gerald Keusch2

1 http://www.wpro.who.int/health_research/policy_documents/global_strategy_may2008.pdf
2 Power point presentation made during 16-18 December, 2014 meeting by Dr Gerald Keusch will be released as technical paper.
5. *Canada’s Contribution to Global Health Research and Innovation* based on *Review Of Canada’s Key Contributions to Global Health Research and Innovation* by Halla Thorsteinsdóttir
Introduction

Member states of our Region requested (in High Level Preparatory Meeting for the Regional Committee, July 2014) to take up an assessment of Global Strategy and Plan of Action on public health innovation and intellectual property (GSPA) so as to inform/assist decision making in WHA in 2015. An assessment of GSPA was mandated by WHA 62 that called upon the public health community “to conduct an overall programme review of the global strategy and plan of action in 2014 on its achievement, remaining challenges and recommendations on the way forward and report to the Assembly in 2015 through the Executive Board” (WHA62.16 para 6).

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To contribute to the discussions on follow up GSPA (WHA61.21) five technical papers from experts relevant to the core of the Global strategy and plan of action on public health, innovation and intellectual property (GSPA-PHI) were presented at the SEAR regional meeting during 16-18 December 2014 in Bangkok for assessment of progress in implementing global strategy and plan of action on public health, innovation and intellectual property (GSPA-PHI) for South East Asia. The papers underscore the importance of R&D, finance, collaboration, innovation, implementation, access collaboration and monitoring for successful implementation of GSPA-PHI. The technical papers include Assessment/Next steps on WHA61.21 - Global Strategy and Plan of action on Public Health, Innovation and Intellectual Property: India Country Profile by Prof N.K. Ganguly. The document assesses the success and challenges faced by SEAR nation in GSPA implementation.

Sri Lanka conducted a systematic national assessment for Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (WHA resolution 61.21) and this is the first assessment of this kind done in any country in WHO.

The Assessment by Sri Lanka was done in several steps. The assessment tool prepared by WHO HQ was introduced to the relevant institutions following which representatives from the institutions participated in a workshop. The findings of the national assessment related to six main sections. They are health research and development, manufacturing of pharmaceuticals, application and management of intellectual property, improve delivery and access, traditional medicine and monitoring and reporting.

The outcome of this assessment leads to the following considerations: Sri Lanka has a national S&T policy and several institutions dedicated to promote R&D in general and health R&D in particular. However, the country has to do much on coordination of R&D efforts to support public health objectives. The available investment of health R&D needs further prioritization. The capacity to

develop health products, particularly pharmaceuticals and related technologies is weak at present. The pharmaceutical sector needs major improvements to support public health objectives. In order to guarantee continuous access to quality medicines and other health products existing processes need to be strengthened further.

The national assessment provided baseline status of the country on research and development (R&D), innovation, intellectual property and access to medical technologies. It is hoped that the understanding gained from this exercise will be useful as a road map for further progress on WHA 61.21 and health R&D goals at national level and global engagement⁴.

⁴ http://www.who.int/phi/implementation/monitoring/Sri_Lanka-report.pdf
Terms of Reference for the present study

1. Preparation of the assessment tool
2. Identifying stakeholders in coordination with the Ministry of health
3. Adaptation of assessment tool for GSPA on PHI and IP for Sri Lankan context and preparation of a guideline for data collection
4. Preparation of consultation of stakeholder list and guiding them for data collection
5. Compilation of data and a draft document for discussion for the workshop to be held during end of April 2014
6. Supporting WCO to organize the workshop
7. To perform any duty, as assigned by WHO SEARO or WCO during the period of APW
Introduction

Sri Lanka agreed to a request of the World Health Organization Regional Office for South East Asia to carry out an National Assessment on a tool on public health innovations and intellectual property. This is part of the follow up action on the World Health Assembly (WHA) resolution 61.21, on Global Strategy on Public Health Innovation and Intellectual Property. This is the first time any country in SEARO has used the National Assessment tool. The assessment is intended to provide baseline status of the country on research and development (R&D), innovation, intellectual property and access to medical technologies. It is hoped that the understanding gained from this exercise will be useful as road maps for further progress on WHA 61.21 and health R&D at national and global levels.
These are in the following order:

1. *Innovation + Access: The Urgent Need for a New Paradigm for Biomedical Innovation* highlights upon the continued ‘fatal imbalance’ between global disease burden and health product development. As the health needs of low income countries and middle income countries are constantly being ignored, them settling for products not meant for them and with out of reach prices calls for a paradigm shift in approach from ‘market driven’ to a ‘need driven’ product development. Thus a multilateral framework for R&D at global level, public leadership, alternative approach to innovation, regional and international collaborations and flow of information among them to ensure affordability and equitable access for all patients is needed.

2. *Principles for developing collaborating networks, academia and public-private partnership engagement for research and innovation – the Africa, Asia and South America context* discusses how there has been a diversification in the type and number of organizations funding, advocating and participating in global health arena. Yet despite the creation of this new landscape the problem of ‘access to’ and equality in improved health care persists. A well-established system of networks, Collaborations and partnerships can propel this landscape into a truly global one.

3. *For Developing a multidisciplinary approach for global health - clinical, epidemiological and basic research: A personal perspective* identifies agenda setting, finance, R&D, implementation and M&E as the core function of any global health system but Dr Keusch then highlights how in the current global system of multiple global actors, these core functions have to be made dynamic and adaptable. These concepts are very much applicable for successful implementation of GSPA-PHI.

4. *National Assessment Tool: To assist member states in implementing the global strategy and plan of action on public health, innovation and intellectual focuses upon assessment and monitoring & evaluation of implementation of GSPA-PHI.* As part of its efforts to implement the GSPA-PHI, the WHO has developed a National Assessment Tool (NAT) based on country-specific action items in the strategy. NAT facilitates a coherent assessment of the environment for medical innovation and how conducive is the national landscape in terms of infrastructure, policies, legislation, regulations and funding. Furthermore the tool helps the countries identify their weaknesses and what type of interventions will be required to overcome them.

5. *Canada’s Key Contributions to Global Health Research and Innovation* follows the start of Canada’s contributions towards global health research. The pattern of budgeting towards global health, paper publications on neglected diseases over the years, collaborations with international institutions and players in the field of health has been cataloged. This paper is a good example of how developed countries can play a crucial role in enabling affordable and equitable access to those in less developed countries. It is also a good example of how Canada has self-assessed its performance on the commitment it has made towards global health and consequently led to a successful implementation of GSPA-PHI.

of how far has India come in implementing the 8 GSPA elements. The document makes a
good case study to understand success, roadblocks and challenges faced by SEAR member
in implementation of the 25 sub-elements.
Innovation + Access: The Urgent Need for a New Paradigm for Biomedical Innovation by Dr Bernard Pécoul, Executive Director, Drugs for Neglected Diseases initiative (DNDi)

1. Introduction

Over the past two decades there has been a growing recognition that the current system for biomedical innovation has failed to deliver adequate and affordable health technologies, particularly for diseases that disproportionately affect poor people. Although there have been several new research and development (R&D) initiatives launched -- including new non-profit models for carrying out neglected disease R&D (such as Product Development Partnerships), new industry R&D platforms, new academic consortia, new incentives mechanisms to induce industry to engage more in neglected areas, as well as slightly increased funding for innovation to fill the R&D gaps for some neglected diseases -- progress has been largely incremental.

An analysis of drug development trends published in 2002 showed that only 1-1% of all drugs approved over the preceding 25 years (1975-1999) were for so-called neglected diseases (including the 17 conditions now classified as neglected tropical diseases by the World Health Organization, tuberculosis and malaria), despite these diseases accounting for 12% of the global disease burden. The deficiency in R&D for neglected diseases documented in the study has also been reported in the area of antibiotics, where new drugs are urgently needed to treat drug-resistant bacterial infections.

In 2012, a new analysis conducted by the Drugs for Neglected Diseases initiative (DNDi), Médecins Sans Frontières (MSF) and others found that of the 850 new drugs and vaccines approved for all diseases between 2000 and 2011, just 4% (37) were for neglected diseases. In addition, of the nearly 150,000 registered clinical trials for new therapeutic products in development as of December 2011, only 1% was for neglected diseases. This highlights the persistence of the ‘fatal imbalance’, described over a decade ago, between global disease burden – and thus patients’ needs – and therapeutic product development.

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9 The Special Programme for Research and Training in Tropical Diseases (WHO-TDR), and three universities (University Hospital of Grenoble, France; Joseph Fourier University, France; University of Oxford, UK)
The lack of medical innovation as well as the lack of access to health tools, including medicines, diagnostics, and vaccines, in low- and middle-income countries have been well-documented, notably by the landmark 2006 report of the WHO Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH), which recommended that governments take concerted action to address the crisis in innovation and access to needed health technologies. The report describes the cycle of innovation as including three major phases, which feed into each other: discovery, development, and delivery. The driving force behind this cycle -- that is, the market-driven expectation of a high return on investment -- has been increasingly recognized as the overriding reason for the failure of the innovation system to deliver appropriate, adapted, and affordable health tools, particularly for low- and middle-income countries and especially among poor, marginalized, and neglected people. The Commission stated “[w]here there is no purchasing power [t]he market alone, and the incentives that propel it, such as patent protection, cannot by themselves address the health needs of developing countries.”

Three fundamental problems with the current medical innovation system are illustrated with three global health crises.

First, global public health needs are not in the driving seat when it comes to R&D priority-setting. Regardless of how great the needs may be, where commercial potential is weak, there is little “pull” to develop new technologies. The Ebola outbreak that has so far claimed more than 5,000 lives illustrates such a market failure. Even though the disease was identified 40 years ago, with regular outbreaks in Africa, the international community is left to fight today’s alarming outbreak with basic medical care, and no approved treatments or vaccines. There are some experimental drugs and vaccines in the pipeline, most of which originate from bio-defense research activities. The poor populations affected by Ebola did not constitute an adequate “market incentive” for the private sector to take the risk of investing into the development of desperately needed medical tools. Governments and international organizations failed to design the necessary framework and incentives to drive the development of such tools, as for many other neglected diseases.

Similarly, the alarming rise in antimicrobial resistance on a global scale without the prospect of new antibiotics in pharmaceutical companies’ pipelines is another case of the failure of the current innovation framework. Governments have to create the necessary financial and regulatory tools to drive research towards public health priorities, as acknowledged in a World Health Assembly resolution adopted on May 2014\(^\text{10}\).

Second, patients in low- and middle-income countries must often “make do” with innovations that primarily cater to patients in high-income countries. Medical tools are too often developed first for these patients, with roll-out in resource-limited settings an afterthought, at best. For instance, even though the majority of patients infected by hepatitis C virus (HCV) live in low and middle income countries, over 80% of clinical studies are held in North America, Europe, and Japan. It is encouraging to have a very robust HCV drug pipeline that potentially will offer greatly improved treatment options in the coming years. However, it remains to be seen whether optimal drug therapy for all genotypes and subtypes can be delivered.

Third, even when there is enough of a profit incentive to drive innovation – for example when diseases affect both developed and developing countries alike – the resulting products are too often priced out of reach. Developing countries are not the only ones to be hit, as ever higher prices for new medical tools strain the healthcare budgets of developed countries as well, posing access barriers to increasing numbers of people. In addition to new drugs to treat HIV or cancer, discussions now focus on the price of newly approved drugs to treat hepatitis C. With a cure rate of over 90%, recently approved direct-acting antivirals (DAAs) could potentially revolutionize individual hepatitis C treatment on a global scale. However, current prices at around USD 1000 per pill, amounting to approximately USD 100000 for a full treatment course, can only lead to treatment restrictions in developed countries, let alone developing countries. Licensing agreements have been signed, preferential prices offered to some countries, but access still has to be waged drug by drug, country by country, and company by company.

Experts from the Bellagio meeting at the Rockefeller foundation in 2012 on the implementation of the WHO Consultative Expert Working Group on Research & Development (CEWG) agreed that\textsuperscript{11}: “[M]arket failures affected all countries, regardless of level of income – such as the growing problem of antimicrobial resistance and the hollow pipeline for new effective antibiotics. While acknowledging that the categories of Type I, II and III diseases were a useful analytical tool to understand why certain diseases attracted more or less private sector investment, the experts recognized that in order to generate long-term public funding from all countries, a new global framework would need to offer some benefits applicable to all countries (and not be arbitrarily limited by disease categories). Therefore, a more useful way of delineating the scope of a new framework was to identify areas of market and/or public policy failure – that is, diseases or areas of technology where the existing system had failed to deliver safe, effective, quality products that were suitable and affordable, particularly for poorer populations.”

After over 10 years of debates and international negotiations, including the adoption and implementation of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA), which endorsed by consensus in 2008 a “strategy designed to promote new thinking in innovation and access to medicines, which would encourage needs-driven research rather than purely market-driven research to target diseases which disproportionately affect people in developing countries” (WHO, 2008), the imperative is more clear and pressing than ever for governments to take concrete actions and spur biomedical innovation in areas neglected by the current innovation system. A new paradigm is urgently needed.

The WHA resolution 66.22 on the follow-up of the report of the CEWG did not take up the key recommendation of the experts to start negotiations on a binding convention (or sustainable global framework) to strengthen financing and coordination of R&D to address unmet medical needs of developing countries. Any discussion of an R&D Convention was to be postponed until 2016. Meanwhile, two significant action points will be handled by WHO and member states: establishing a Global Health R&D Observatory under the auspices of WHO, and asking the WHO Director General to set up several ‘demonstration projects’.

\textsuperscript{11} Multi-stakeholder Technical Meeting on Implementation Options Recommended by the WHO Consultative Expert Working Group on Research & Development (CEWG): Financing and Coordination at the Rockefeller Foundation Bellagio Center, 16–19 October 2012
The specific action point called “demonstration projects” of the resolution adopted WHA 66th 12, specifies that demonstration projects should in particular “utilize collaborative approaches, including open knowledge approaches for R&D coordination; promote the delinkage of the cost of R&D from product price; and propose and foster financing mechanisms including innovative, sustainable and pooled funding”, and in addition to “provide evidence for long term sustainable solutions”.

Consequently, the mid-term and final outcomes of the demonstration projects must contribute to paving the way for continuous shaping of the discussion on a sustainable global framework knowing that the outcomes should be relevant for type I, type II, and type III diseases and not only for type III diseases 13, which is the current scope of the projects selected.

In this global context of ten years of negotiations and numerous innovative experiments and reports, WHO and Member States have the unique opportunity to establish a multilateral framework of principles and rules regulating R&D that will ensure patient needs are at the core of R&D efforts, that will maximize global health impact, and, importantly, that will ensure affordability and access for all patients in need.

After a decade of experience and lessons learned building an alternative model for innovation for neglected diseases, and after delivering six new treatments while also building a robust pipeline for some most neglected diseases, DNDi can share key features of its approach to R&D, which may be helpful in larger discussions about how to best design R&D strategies that will address unmet patients’ needs that predominantly or exclusively affect people in low and middle income countries.

2. Drugs for Neglected Diseases initiative (DNDi) and key features of an alternative R&D model designed to address unmet patients’ needs

Created in 2003, the vision of DNDi is to improve the quality of life and the health of people suffering from neglected diseases by using an alternative model to develop drugs for these diseases and by ensuring equitable access to new and field-relevant health tools.

Considering public leadership as a critical component of a sustainable alternative approach to innovation and access for diseases and populations that the market has failed, DNDi was

12 Decision point A66/B/Conf./2 adopted at the World Health Assembly 66th
13 The Commission on Macroeconomics and Health (CMH) distinguishes between three types of diseases.
   • Type I: incident in rich and poor countries with large vulnerable populations in both areas. These diseases attract sufficient R&D (both public and private) but poor country access to medicines may be restricted as they are often patented and expensive.
   • Type II: incident in rich and poor countries, but with a much greater incidence in poor countries, such as HIV/AIDS and TB. R&D incentives exist in the rich countries, but the level of spending is very low compared to global disease burden.
   • Type III: incident almost exclusively in poor countries. These are known as extremely neglected diseases, e.g. African sleeping sickness and river blindness. R&D in rich countries is almost non-existent and new treatment developments are usually fortuitous or accidental discoveries.
established by Médecins Sans Frontières/Doctors Without Borders (MSF) with four public institutions from endemic countries such as the Oswaldo Cruz Foundation (FIOCRUZ) of Brazil, the Indian Council of Medical Research (ICMR), the Kenya Medical Research Institute (KEMRI), the Ministry of Health of Malaysia, in addition to the Institut Pasteur and The Special Programme for Research and Training in Tropical Diseases (WHO-TDR) as a permanent observer.

Within the first 10 years, the initiative has already delivered six new treatments and established a solid pipeline, including 12 new chemical entities (NCEs) in preclinical and clinical development. Acting as a “conductor of a virtual orchestra,” DNDi leverages partners’ specific assets, capacities and expertise to implement projects at all stages of the R&D process. Over 350 collaborations in 43 countries, including nearly 20 pharmaceutical and biotechnology companies, and over 50 universities and research institutes have been put into action. North-South and South-South technology transfer projects and several disease specific clinical research platforms in endemic regions with national programs and scientific partners & clinicians from theses respective endemic regions were formed to strengthen research capacity in neglected disease-endemic countries.

Several distinctive features of DNDi’s not-for-profit drug development model would seem to be also key components of a global framework, namely:

- a patient-centred, needs-driven approach;
- the leveraging of existing knowledge and expertise by building solid alliances with public and private partners, especially in endemic countries;
- secure equitable access to treatment for patients;
- open innovation models reduce duplication and costs of R&D;
- innovative regulatory pathways needed to ensure timely patient access to treatments, reduce total costs of delivering treatments;
- leadership of disease-endemic countries in the coordination of R&D, especially in defining based on patient needs and in allocating resources to identified priorities;
- new sustainable financing mechanisms necessary to provide adequate, predictable funding, and to ensure public responsibility in addressing global health R&D needs.

a. A patient-centered, needs-driven approach

Beginning the R&D process with the end in mind, and keeping it in mind until patient needs are addressed appropriately, is engrained in the way the organizational model of DNDI is designed. Disease-specific target product profiles (TPPs) guide and determine all R&D activities. A succinct description of the ideal specifications needed for a specific treatment, considering the needs of the patients and the practical conditions in which most patients will be treated, these TPPs are

14 The six new treatments are two fixed-dose antimalarials (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 paediatric dosage form of benznidazole for Chagas disease.
15 DNDi has helped establish three clinical research platforms: Leishmaniasis East Africa Platform (LEAP) in Kenya, Ethiopia, Sudan, and Uganda; the HAT Platform based in the Democratic Republic of Congo (DRC) for sleeping sickness; and the Chagas Clinical Research Platform in Latin America.
developed with leading experts from endemic countries, researchers, clinicians, disease control program managers, WHO, and patient representatives whenever possible.

b. **Leveraging of existing knowledge and expertise through solid alliances with public and private partners, especially in endemic countries.**

To fill up R&D gaps in drug development, there is obviously not a single innovative solution. DNDi manages every phase of the drug development process – from drug discovery and pre-clinical research, to clinical trials and large-scale implementation studies – by articulating multiple alliances, thus ensuring the best possible alignment of partners in fulfilling the objectives set in the TPP. In so doing, DNDi serves as a conduit of information between and among partners, and has been instrumental in strengthening cross sector networks.

This requires two critical components: constant and strong involvement of authorities and partners in endemic countries to help define priorities and facilitate implementation of new tools, on the one hand; and solid alliances with pharmaceutical and biotechnology companies and academia through innovative IP licensing to access sources of knowledge in order to identify potential new compounds and ultimately reduce the cost of development, on the other hand.

c. **Secure equitable access to treatment for patients**

Any public health needs’ driven R&D model is guided by the need to ensure that drugs are affordable and accessible in an equitable manner to patients who need them. Licensing terms can provide that (1) publicly funded research and the outputs of such research are public goods and (2) that the price of the final product must therefore be affordable, through delinkage from R&D costs. This is possible if R&D is not financed through IP rent revenues, but by multiple sources of primarily public funding. Over the years, DNDi has been able to negotiate favourable licensing terms with many companies, and has come to define a set of “gold standard” terms, which includes:

- Perpetual royalty-free, non-exclusive, sub-licensable licenses in the specific disease areas determined in the contract;
- Worldwide research and manufacturing rights;
- Commitment to make the final product available at cost, plus a reasonable margin, in all endemic countries, regardless of their income level;
- Non-exclusivity, enabling technology transfer and local production to multiply sources of production and decrease cost of product.

Initiatives aiming to facilitate access to IP, such as the Medicines Patent Pool (MPP) for HIV, should be further encouraged and supported.
d. **Open innovation models reduce duplication and costs of R&D**

As demonstrated by the Open Source Drug Discovery consortium in India, ChEMBL-NTD, WIPO Re:Search, the Medicines for Malaria Venture’s open access Pathogen Box or GSK’s Open Lab, initiatives for open innovation are flourishing, and while it may be too early to evaluate their impact, they are a clear illustration of a trend toward a more open approach to boosting innovation.

Health R&D to address unmet needs requires new innovative licensing models as well as open models for sharing knowledge and research data. R&D strategies based on open innovation models are critical to boost innovation globally, reduce duplication and costs of R&D, and speed up delivery of new medicines to patients. DNDi estimates its costs of development to range from EUR 10-40 million for an improved treatment, and EUR 100-150 million for an NCE including attrition rate but not in kind. Although it is difficult to compare costs of development between different business models, the first 10 years of DNDi’s experience indicate that innovative R&D models can both deliver rapidly for patients and potentially be more efficient than the traditional pharmaceutical business model. This may be explained by the more open, collaborative modus operandi, the emphasis on leveraging expertise from a wide range of partners in a non-competitive way, and the fact that DNDi first products capitalized on low-hanging fruits.

e. **Innovative regulatory pathways are needed to ensure timely patient access to treatments, reduce total costs of delivering treatments, and ultimately support greater capacity strengthening in disease-endemic countries**

Innovative regulatory pathways are needed to expedite access to essential medicines in developing countries, while ensuring that new treatments are safe, effective and of quality, and reduce costs linked to regulatory approvals, while strengthening local regulatory capacity.
In addressing developing countries’ health needs, the argument that Western regulatory authorities are the only certified sources to evaluate the quality, safety, and efficacy of medicines should be challenged, in particular for assessing the risks and benefits of health products for diseases predominant in developing countries, for which therapeutic options are often severely limited.

It is urgent to strengthen capacities of poorly resourced regulatory bodies in developing countries notably through enhanced formal collaboration with regulatory bodies of well-resourced and experienced drug regulatory authorities particularly in endemic countries or of so-called ‘stringent’ regulatory authorities, in partnership with WHO Prequalification Programme. It is fundamental to stimulate, support, and promote ongoing regional initiatives that aim at accelerating scientific risk/benefit adjusted reviews and rationalise mutual recognition of regulatory policies within regional zones where disease prevalence is similar.17

17 For instance with support from WHO, the African Medicines Regulatory Harmonization (AMRH) initiative set up with Regional Economic Communities (RECs) to increase access to good quality, safe and effective medicines through harmonizing medicines regulations, and expediting registration of essential medicines.
f. Leadership of disease-endemic countries in the coordination of R&D, especially in defining priorities based on patient needs and in allocating resources to identified priorities.

The sustainability of essential health innovation and access critically depends on public leadership in defining needs and setting R&D priorities under WHO coordination. It also depends on Governments’ role in prioritizing research and designing adequate national policies to ensure treatment access for patients.

The CEWG report identified inadequate coordination and priority-setting as an important weakness in the existing global R&D system and recommended pooling at least 20% of national funds through an international mechanism.

The set-up of a Global Health R&D Observatory under the auspices of WHO represents an important first step for prioritizing global health R&D needs and gaps. A well-managed and transparent Observatory will be essential, especially if funding pools become established. So far there has been no inter-governmental, politically legitimate system for R&D priority-setting at the global level, so an Observatory would be a key starting point. While by itself an Observatory will not address all of the challenges posed in the CEWG report, WHO member states should allocate resources to ensure that a Global Health R&D Observatory can function. At a minimum, the observatory should perform two critical functions: one that is primarily technical (monitoring) and one that is more “political,” namely, priority-setting and coordination. In regard to priority setting, the structure, governance, and accountability mechanisms are critical and need to be carefully designed.  

In addition, the set-up of a pooled fund for health R&D hosted by WHO/TDR, as agreed to consider by WHO Member States,  
could facilitate additional commitments from public funding from a wide range of traditional donors as well as emerging economics and other low- and middle-income countries. Financial participation of pooling would not only facilitate coordination, but could also help ensure that global public priority-setting processes would be matched with at least some financial resources.

New sustainable financing mechanisms and increased resources are necessary to provide adequate, predictable funding, and ensure public responsibility in addressing global health R&D needs.

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19 WHA67(15) point (4) noted, without prejudice to future discussions in the context of recommendations of the Consultative Expert Working Group on Research and Development Financing and Coordination and actions on other sustainable mechanisms for financing health research and development, the assessment made by the Secretariat and the possibility of using an existing mechanism to host a pooled fund for voluntary contributions towards research and development for type III and II diseases and the specific research and development needs of developing countries in relation to type I diseases”. http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_DIV3-en.pdf  
Diversification of funding is necessary to prevent unhealthy influence by or dependence upon any single donor. Independence is particularly important in building and managing the project portfolio; prioritizing R&D projects; and in assessing significant unmet patient needs, R&D opportunities, potential partners, and potential sources of funding.

The G-FINDER report “Neglected disease R&D: A five-year review” indicates that while the public sector provides nearly $2 billion each year, or two-thirds of all research & development (R&D) funding for neglected diseases, government funding has continued to move away from product development and towards traditional basic research.” 21 Outside the United States and United Kingdom, the remainder of the world’s governments combined currently provides less than one-third (less than $1 billion) of all neglected disease R&D funding.

As recommended by a recent report from an Institute of Medicine-convened task force in 2013 22 “there is an opportunity to considerably expand government funding from other European governments, in addition to some of the very important emerging economies, including “BRICS” countries (Brazil, Russia, India, China, and South Africa), as well as Japan, several Middle Eastern countries (Hotez, 2010), the “MIST” economies (Mexico, Indonesia, South Korea, and Taiwan), and other middle-income nations in Latin America and Asia, which could also make major contributions to research.”

Also, building upon the successful model of UNITAID, which is financed through airline ticket taxes, indirect tax proposals on financial transactions, or sectorial taxes such as tobacco, digital, or mobile phone taxes could constitute the type of innovative and sustainable funding mechanisms that are needed. The GHIT mechanism as well set up in Japan throughout a consortium in between Japanese governments (MOH and MFA), the Bill & Melinda Gates Foundation and five pharmaceutical industries is an another model for resources mobilization.

Commitment of governments, both traditional donors and low-and-middle income countries, notably through partnerships and through innovative financing mechanisms, is crucial to compensate for the market failure in drug development and to fulfill current financing gaps.

3. Conclusion

Ten years after the adoption of the GSPA, the glaring lack of an effective drug or vaccine to help control the Ebola epidemic in West Africa, the crisis in access to hepatitis C treatment, and the

21 Moran M, Guzman J, Henderson K, et al. Neglected disease research and development: a five year review. G-FINDER 2012. Policy Cures. http://www.policycures.org/g-finder2012.html. (accessed June 18, 2013). Previous studies: the estimate by the Commission on Health Research for Development was that, in 1986, $1.6 billion of $30 billion R&D worldwide was addressed to problems of the developing world. A similar study carried out at Harvard University in 1995 suggested that, in 1992, $2 billion of a worldwide $56 billion in health research was directed at the problems of the developing world.


increasingly alarming and global threat of antimicrobial resistance desperately illustrate that a much more ambitious approach to reforming the current innovation system is needed. This must start with more coordinated and sustainable public leadership: governments and WHO should channel the efforts of all actors towards clearly defined goals for needs-driven innovation and must no longer accept the trade-off between innovation and access offered by the current R&D system. Medical innovation must aim to change practice, for the benefit of patients. But ideas, knowledge and inventions can only benefit patients who have access to the fruits of innovation. What is needed, therefore, is not just innovation – but both innovation and access. The assessment of the GSPA is an opportunity to continue to work towards those goals.

There has been some progress with regard to elements 1 and 2 of the GSPA on prioritization and promotion of R&D, with the creation of the global health R&D observatory and the development and delivery of several health tools for neglected diseases launched or under development by non-profit product developers and other relatively new R&D initiatives.

Similarly, innovative capacity (GSPA element 3) is being built and improved through such collaborative projects. However, most of these organizations remain very fragile and dependent on public or philanthropic funding and private sector goodwill. A more ambitious, coherent global framework is needed to sustain such progress. Incentive models and sustainable funding are also critically needed to support transfer of technology (GSPA element 3), which remains too scarce.

Lessons from various new initiatives may be useful in assessing element 4 of GSPA, i.e. the application and management of intellectual property to contribute to innovation and promote public health. As shown by other recent initiatives (e.g. the Medicines Patent Pool), IP can be managed in a manner that does not impede equitable and affordable access to the end-products, nor impede additional or follow on research. Governments have the responsibility to regulate the health market, through models that delink R&D costs from products prices, to ensure both innovation and access.

DNDi and other PDPs such as Medicines for Malaria Venture (MMV) experience over the past ten years have shown that it is possible to address the needs of the poorest populations by developing quality, adapted, and affordable new health technologies, notably through the identified key components for success developed in part 2. These examples could serve as useful guidance for policy makers who need to identifying new approaches for the next decade to address unmet patients’ needs that predominantly or exclusively affect people in low and middle income countries:

- put the specific needs of patients upfront, at the start of the innovation process;
- break the link between the cost of R&D and the price of products;
- ensure that the fruits of innovation are accessible and affordable;
- integrate global health R&D monitoring, coordination, and financing;
- strengthen and harmonize regulatory capacities in endemic regions to facilitate implementation of new health technologies.
However, these efforts will not be transformed into sustainable change if the foundations for a new global framework that stimulates essential health R&D are not laid. This is what is really at stake today and for the future: to generate public health breakthroughs it is mandatory to consolidate sustainable public and private partnerships, notably with partners from endemic countries; and to ensure further development and advance promising technologies of unmet patients’ needs, increased and innovative funding as well as new incentives are needed.

Bernard Pécoul, MD, MPH, Executive Director, DNDi

Dr Bernard Pécoul has led DNDi (Drugs for Neglected Diseases initiative) since its foundation in 2003. Under his guidance, DNDi – a not-for-profit research and development organization – and its partners have built the largest-ever R&D portfolio for kinetoplastid diseases (leishmaniasis, sleeping sickness, and Chagas disease) as well as developing treatments for malaria. In 2011, DNDi extended the scope of its portfolio to include specific helminth infections and paediatric HIV. Since its inception, DNDi has delivered six new treatments through partnerships with public and private organizations worldwide, and aims to deliver a total of 11 to 13 new field-adapted treatments for neglected diseases by 2018.

Prior to DNDi, Dr Pécoul was Director of the Médecins Sans Frontières (MSF) Campaign for Access to Essential Medicines from 1998 to 2003, a position he took on after that of Executive Director of MSF-France. While working with MSF, Dr Pécoul carried out field missions in Africa, Latin America, and Asia. In 1988, he co-founded Epicentre, an MSF-affiliated NGO specialized in epidemiology.

After obtaining his medical degree at the University of Clermont-Ferrand, France, Dr Pécoul earned a master’s degree in public health at Tulane University, USA. In 2012, he was awarded an honorary Doctor of Laws Degree by the University of Dundee, UK.

Bernard Pécoul is member of the Joint Coordination Board of the Special Programme for Tropical Disease Research (WHO/TDR) and a board member of Unitaid’s Medicines Patent Pool Initiative.

About DNDi

The Drugs for Neglected Diseases initiative (DNDi) is a not-for-profit research and development (R&D) organization working to deliver new treatments for the most neglected diseases, in particular sleeping sickness (human African trypanosomiasis), Chagas disease, leishmaniasis, filaria, and paediatric HIV/AIDS. Since its inception in 2003, DNDi has delivered six new treatments: two fixed-dose antimalarials (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 paediatric dosage form of benznidazole for Chagas disease. DNDi was founded by Médecins Sans Frontières/Doctors without Borders (MSF), Indian Council of Medical Research, Kenya Medical Research Institute, Brazil’s Oswaldo Cruz Foundation, Ministry of Health of Malaysia, and Institut Pasteur in France, with the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) as a permanent observer.
Principles for developing collaborating networks, academia and public-private partnership engagement for research and innovation – the Africa, Asia and South America context

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1: Introduction

Over the past 15 years there have been significant but uneven changes in global health that have often failed to address the problems of access to improved treatments, of healthcare for patients and populations, and of equality. Some of the most significant changes have been in the number and diversity of organisations involved, the level of funding available, the number of players participating and the level of advocacy and the opportunity to make an impact. A new landscape has been created with major progress accompanied by the development of new tools for treatment and prevention of diseases. This challenge is now to integrate the landscape of players (see section 1) better and establish a legacy of a sustainable model for global health.

In this paper we address part of this change: the principles for developing successful collaborating networks and partnerships, the engagement of academia, public-private partnerships and the private sector in research and innovation. We focus on infectious diseases in Africa, Asia and South America contexts. We discuss the interactions between those involved in Research and Development (R&D) around of diagnostics, drugs and vaccines), and those who are involved in the implementation of tools, policy and practice. Whatever the nature of the interactions, it is essential to understand the reasons for success and failure, that lessons learned are not only communicated to the funders, but also to the ministries, the health workers and populations affected. We describe some of the principles for developing clear and positive interactions and collaborations, and then show, with selected examples, how these have had an impact on global health, innovation and intellectual property.
2: The Landscape of current participants in global health and innovation

A full documentation of the current network of partnerships (as at November 2014) is beyond the scope of this paper, but the essential interactions can be outlined (Fig. 1). This network includes public organizations (e.g., international organizations, government, academia and research institutions), private non-profit-organizations (e.g., NGOs, philanthropic organizations, foundations, civil society, public-private partnerships) and private for profit organizations (pharmaceutical and biotechnology companies).

Figure 1: The R&D Landscape – some players and partnerships

However, to bring a new health care tool or system to effect, it is essential to consider both R&D and implementation as one continuous process. A clear lesson learned from many projects over the past decades is that whether starting from a new concept of health delivery (tool or system), or from the identified need for patients of health systems, the complex R&D and implementation pathways must be seen as a bi-directional process (4) (Fig. 2). For example, discovery and innovation have one suite of drivers, participants, outcomes and measures of impact but the context for treatment and improved healthcare, patients and population needs within a specific environment (economic, social, ecological) and health systems have another suite of drivers, participants and measures of impact. The understanding of the latter should set the framework for the former. One method that tried to encapsulate this approach is the Target or Clinical Product profiles (TPP) or Certificate of a Pharmaceutical Product (CPP), used by many organisations and companies involved in R&D [Box 1].
Box 1: Target Product Profile (TPP) for Malaria (5)

A living reference document for an R&D project recommended by the US Food and Drug Administration (FDA) for summarizing a clear and tangible focus, and the latest information about the intended product characteristics and use.

Examples (6): The following two brief profiles of TPP are summaries of what an ideal malaria treatment should look like.
- Single Exposure Radical Cure and Prophylaxis (SERCaP): A single dose combination therapy that radically cures all malaria species and stages.
- Single Exposure Chemoprotection (SEC): A single dose therapy that provides lifelong protection against all malaria species

As suggested by the FDA, “The TPP embodies the notion of beginning with the goal in mind” (5). If the goal in mind embodies notions of a one day course of treatment (e.g. for malaria), or to detect a central nerve system infection (e.g. sleeping sickness), or treatment/administration within health centres lacking a cold-chain, then the decisions about what type of product needed or the way the new treatment is administrated should start within the discovery process involving lab scientists and clinicians through to implementation, which may require social scientists and health workers. The present emphasis on innovation and discovery needs to be balanced with innovative new approaches for engaging local healthcare workers and systems, patients and populations.
Notably a network of participants during the past 15 years, public-private partnerships (PPPs), has become a successful mechanism for the development and introduction of new drugs, vaccines and diagnostics (7). The term PPP covers “a wide variety of ventures involving a diversity of arrangements, varying with regard to participants, legal status, governance, management, policy-setting prerogatives, contributions and operational roles” (8). Although PPPs in health are not new, indeed the WHO Special Programme for Research and Training in Tropical Diseases (WHO TDR) has operated on this basis for the past three decades, they have a highly variable in structure and intent and all have different proportions and roles for the public and private sector participants (9). They can range from small, single-product collaborations, to large consortia involving industry, and from not-for-profit organizations to for-profit companies (4).

A central role in the transformation of the landscape has come through the establishment of Product Development Partnerships (PDPs) (Fig. 1) (10). Since 1999 several of these organisations have taken new “tools”, for infectious diseases, where profit-alone is insufficient to engage key players, through development and delivery to populations in African, Asia and South America [Box 2]. Several PDPs have established a portfolio approach, that allows unfeasible projects to be dropped or more promising ones to be advanced and that permit decisions based on strengths and liabilities and to anticipate the need for back-up projects. PDPs also work with multiple partners, involving another set of skills collaborations and partnerships. These kinds of partnership are

quipe.

exemplified by, for example Medicine for Malaria Venture (MMV) with the pharmaceutical industry and Drugs for Neglected Diseases initiative (DNDi) with clinical platforms in disease endemic countries (DECs) in Africa, Asia and South America [Box 2]. In Southeast Asia a successful partnership has been established in Singapore called namely Novartis Institute for Tropical Diseases (NITD). A recent initiative in Asia, the Global Health Innovative Technology Fund (GHIT), itself a PPP, seeks to engage Japanese industry and academia in R&D for diseases of poverty (DoPs) and neglected infectious diseases (NIDs) [Box 3]. Vector control is also a part of the PDP landscape, with Vector Control, Saving Lives (IVCC) providing a catalyst for the development of new insecticides. Significantly, the lead provided by PDPs has helped to re-stimulate engagement of the private sector in DoPs and NIDs. Innovation around PDPs continues; current interest focuses on Open Source projects, including Open Source Drug Discovery (OSDD) in Asia, and a growing focus on access issues. These changes could not have happened without significant new sources of funding (Fig. 1). A leading role has been played by the Bill and Melinda Gates Foundation (BMGF) and several government organisations (11).

Box 2: PDP model, the Drugs for Neglected Diseases Initiative (DNDi) (12)

- PDP launched in 2003, based in Geneva, Switzerland
- Objective: “To deliver a total of 11 to 13 new treatments by 2018 for leishmaniasis, sleeping sickness, Chagas disease, malaria, paediatric HIV, and specific helminth infections and to establish a strong R&D portfolio that addresses patient needs”
- Partners: Seven institutions including partners from endemic countries including the Indian Council for Medical Research (ICMR), the Kenya Medical Research Institute (KEMRI) and the Malaysian Ministry of Health

Examples (13): DNDi takes an approach that improves the local R&D capacities by using and strengthening exiting capacities for programme implementation, with the launch of three clinical platforms for specific diseases in Africa and South America:

- Leishmaniasis East Africa Platform (LEAP, 2003)
- Human African Trypanosomiasis Platform (HAT, 2005)
- Chagas Platform (2009)

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25 MMV: Medicines for Malaria Venture (PDP based in Geneva, Switzerland), http://www.mmv.org/

26 DNDi: Drugs for Neglected Diseases Initiative (PDP based in Geneva, Switzerland), www.dndi.org/

27 NITD: Novartis Institute for Tropical Diseases (PDP based in Singapore), http://www.nibr.com/research/developing_world/NITD/

28 GHIT: Global Health Innovative Technology Fund (PPP based in Tokyo, Japan), https://www.ghitfund.org/

29 DoPs: Diseases of Poverty (A collective term for describing diseases, disabilities and health conditions that are prevalent among the poor, e.g., HIV/AIDS, Malaria and TB)

30 NIDs: Neglected Infectious Diseases (Infectious diseases that affect populations in low income settings, but has been neglected due to the absence of financial return for pharmaceutical and biotech companies and a failure of public policy to establish sufficient enabling policies).

31 IVCC: Vector Control, Saving Lives (PDP based in Liverpool, United Kingdom), http://www.ivcc.com/

32 OSDD: Open Source Drug Discovery (PPP based in India), www.osdd.net

33 BMGF: Bill & Melinda Gates Foundation (Private foundation based in Seattle, USA), http://www.gatesfoundation.org/
Box 3: The Global Health Innovative Technology Fund (GHIT) (14)

- The first PDP developed in Japan in 2011
- Objective: “To generate novel health technologies (drugs, vaccines and diagnostics) for NTDs that are appropriate, effective, affordable and easy-to-use in the developing world”
- Partners: The public sector (Ministry of Health, Labour and Welfare, Ministry of Foreign Affairs of Japan), the private sector (Five leading Japanese pharmaceutical companies), an international philanthropic foundation (BMGF), and UNDP.

Larger national and international organisations, for example the National Institutes of Health (NIH 34) and the European Union (EU), have also played important roles in funding and building new organisations to deliver tools for global health. One EU initiative involving the private sector, Innovative Medicines Initiative (IMI 35) and the project “New drugs for bad bugs (ND4BB)” for example, has taken one approach to engage both private and public sectors in Europe to address antibiotic resistance. The EU has also led another initiative to bridge the gap between product, practice and policy with the establishment of the European and Developing Countries Clinical Trials Platform (EDCTP 36) which funds clinical trials, from phase 1 to phase 4, for both DoP and NIDs in sub-Saharan Africa [Box 4]. This has required interactions between public organisations and Ministries of Health in DECs, the clinical research community in Europe and Africa, PDPs and pharma/biotech sector, with EU donors.

Box 4: The European and Developing Countries Clinical Trials Partnership (EDCTP) (15)

- EU funded partnership based in the Hague, Netherlands launched in 2003
- Objective: “To accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against HIV/AIDS, tuberculosis (TB) and malaria, with a focus on phase 2 and 3 clinical trials in sub-Saharan Africa”
- Partners: The EU states, Norway, Switzerland and African countries.
- To conduct demand-driven research and ensure active involvement and joint ownership of the programme, the EDCTP has developed a system where a group of scientists and representatives from the regional health bodies, the Developing Countries Coordinating Committee (DCCC), serves as an advisor group.

One of the criticisms of the current PDP and PPP model is the low representation of the DECs within an organization’s decision-making body. The low capacity of the DECs for conducting R&D and clinical trials has been an issue for their limited ownership over R&D programmes. The ASEAN Network for Drugs, Diagnostics, Vaccines and Traditional Medicines Innovation (ASEAN-NDI 37) launched in 2013 is an example of an organization that has a potential to influence this current power dynamic by improving the regional R&D capacity building and thus ownership through tech transfer and education of qualified experts (16).

34 NIH: National Institutes of Health (American biomedical research facility based in Washington, USA), http://www.nih.gov/
36 EDCTP: European and Developing Countries Clinical Trials Platform (EU funded partnership based in the Hague, Netherlands), http://www.edctp.org/
37 ASEAN-NDI: ASEAN Network for Drugs, Diagnostics, Vaccines and Traditional Medicines Innovation (PPP based in Southeast Asia), http://www.asean-ndi.org/
Medicine Patent Pool (MPP 38) set up by UNITAID39 in 2010 is a good example of organizations that take an innovative approach to facilitate access to new or existing health technologies employing traditional intellectual property (IP) tools, particularly licensing mechanisms. It does not challenge the IP positions of incumbents, but find creative solutions to make the innovations protected by that IP available to larger populations. In particular, it facilitates access to HIV/AIDS medicines by enabling generic, low-cost production of pharmaceuticals covered in the developed world by extensive IP rights. Patent pools like MPP do not alter the traditional function of patents, but they create a framework for licensing innovations in a manner that facilitates their low-cost manufacturing and distribution.

At the other end of the bi-directional pathway is implementation. Over the past few years, some PPPs began to favor an inclusive business model that covers from discovery to scaling up of access to medicine. For example, the Pediatric Praziquantel Consortium 40 supported by the GHIT Fund aims to develop tablets for treating schistosomiasis that are suitable for use in very young children living in the DECs (17). When most of the past R&D activates focused on developing a product that is widely applicable, such a recent movement that emphasizes on the importance of applying the local needs in product design is expected to drastically improve the access.

PATH41 is one of the pioneer PDPs that is strong in developing a partnership with the governments of DECs. They also have programmes that are set up independently from their R&D activities for health system strengthening and local capacity building (18). GAVI Alliance 42, another pioneer PDP for vaccines also focuses its activities on health system strengthening by employing a co-funded immunization model. This model encourages the DECs to determine their own health needs and to apply for the funding thus ensuring their ownership and sustainability of the programmes. The Public Health Foundation of India (PHFI 43) based in India is another example of an organization that focuses on local capacity building with an emphasis on advancing public health researches and its implementation at the national level. The Access to Medicine Index report (2014) also identified programmes with the similar focus run by major international pharmaceutical companies (19): For example, Novartis International AG (Novartis 44) started a Healthy Family Programme in India, Kenya, Vietnam and Indonesia as a health education program with a special focus on disease prevention and awareness building of the poor.

What we highlighted here are examples of organizations involved in R&D and some of the major changes that have occurred during the past decade. As discussed, the scope of activities of the organizations involved is complex and it is not always possible to categorize them by a single function. In order to enhance innovation, not only in R&D, but also for implementation activities, coordination and stewardship of all of the organizations and programmes involved is necessary to limit any duplication and waste of resource and to provide coherence to the overall strategy.

38 MPP: Medicines Patent Pool (UN-backed organization based in Geneva, Switzerland), http://www.medicinespatentpool.org/
40 PPC: Pediatric Praziquantel Consortium (PDP led by Merck Serono), no website available.
41 PATH: (PDP based in Seattle, USA), http://www.path.org/
42 GAVI Alliance: Gavi, the Vaccine Alliance (PPP based in Geneva, Switzerland), http://www.gavi.org/
43 PHFI: Public Health Foundation of India (PPP based in India), http://www.phfi.org/
44 Novartis: (Pharmaceutical company, based in Basel, Switzerland), http://www.novartis.com/
Uniting to combat NTDs was launched in 2012 following the London Declaration on Neglected Tropical Diseases was established with an aim to function as an umbrella group to support R&D activities for them to follow the WHO Roadmap. G-Finder is an example of an open-source with data on R&D expenditure on DoPs and NIDs that provides us with an overall picture of where funding gaps lie and how investments are alighted to each other. However more efforts and investments are needed for its coordination in order to further expand the impact of R&D and innovation in global health.

3. The principles for networks, collaborations and partnerships for research and innovation

The principles for building collaborative relationships for research and innovation are clearly dependent on both the partners and the endpoints. Innovation is a catchall term, with different meanings for those involved. For governments research and innovation is about strengthening economic growth, for public health organisations like the WHO it is part of the pathway to Impact, whereas for the private sector the development of pre-competitive models for innovation is to replenish the product pipeline (Figure 3). All organisations in global health rely upon multi-disciplinary teams that often cross-institutes and countries to deliver products. Although dependency between partners in networks, collaborations and partnerships, the constant factor is the need for shared vision, strategy and objectives; without these nothing works and the essential trust can be missing.

For academic researchers engaging in this field, there are key messages for working in these collaborations:

(i) The need to adopt a multi-disciplinary approach is not an option, and there is a need to escape from academic silos
(ii) That research impact is about publication in high citation, high index journals and also about impact and IP. That is there IP to register? How will this be translated in a product? Are there any potential links to be made that change policy and practice?
(iii) An effort is required to understand the culture and standards of the private sector, which ranges from direction of focus, how decision makings are made, devolution of responsibilities management and performance related promotion
(iv) Academics and their institutions are often required to lead in consortia and need to understand the basis for consortium agreements ranging from IP, communications to publications policies
(v) Project management skills are required by key members in the team, or an experienced project manager is appointed with a clear role described
(vi) University Technology Transfer Offices need to move beyond patent-centric metrics to measure the value and impact of scientific research.

46 London Declaration on Neglected Tropical Diseases: (A collaborative eradication programme for NTDs based in London, UK), http://unitingtocombatntds.org/resource/london-declaration
47 WHO Roadmap: A comprehensive plan to control and eliminate 17 NTDs listed by the WHO, published in 2011.
48 G-Finder: (Open source database), https://g-finder政策信息.org/gfinder
Similarly researchers in the private sector need to relate to the pressures operating on their academic partners. Many researcher leaders in the private sector also have a PhD and academic experience. They therefore should understand the essential demands on an academic and their career needs:

(i) To be engaged in peer review in order to gain respect, including invitations to present at national and international meetings;

(ii) To publish in high citation journals in order to obtain substantial external grant income;

(iii) To expand the knowledge base in a given area and tackle riskier aspects of research;

(iv) To understand and tackle IP issues upfront as a way of creating a space for “pre-competitive” or IP-free collaboration, rather than seeing IP as an instrument to constrain and manage the content of the collaboration.

Although for the looser networks, where the like-minded interact and offer mutual support and shared platforms, detailed agreements are not required, in contrast, for partnerships clear policy around communications (including the website, twitter and other social media methods) and publications are necessary. There are many models of “consortia” styled agreements that are available; it is a requirement that all partners sign up to these at the start of the project or programme. Common points normally include:

- Provide the rules for the internal organisation and management of the project including voting regulations;
- Set out how the funding will be distributed by the coordinator;
- Detail provisions about the ownership and licensing of intellectual property, and the dissemination of results;
• Lay out procedures for settling internal disputes;
• Confirm how matters of liability and confidentiality will be handled; and
• Set out how withdrawing and defaulting partners will be addressed.

The creation of collaborative networks for research and development activities, and in particular the collaboration of academic and corporate research groups, has been supported by several innovations in the area of IP. Many of these innovations create “pre-competitive” spaces or consortia, within which actors – pharmaceutical companies and academic research groups in particular – agree not to enforce existing IP rights and/or not to create new ones. A classic example of “pre-competitive” R&D is the model implemented by the Structural Genomics Consortium (SGC 49). Under this model, pharmaceutical companies agree to pool resources (compounds, data, and know-how) and collaborate on high-risk elements of the R&D process – in this case the determination of protein structures for drug discovery. All the data and tools generated through this research are then made freely available to the international scientific community. For-profit organizations retain the ability to pursue competitive, IP-protected projects further down the development pathway. The SGC has used this model to foster research on diseases with global health relevance, and is extending the threshold of pre-competitiveness all the way to the proof-of-clinical-concept stage in the R&D process.

GlaxoSmithKline plc (GSK 50)’s “Open Lab” foundation at its Diseases of the Developing World (DDW 51) group in Spain is another example of a space made for collaboration between pharmaceutical and academic researchers that is sustained by a commitment to facilitate access to proprietary assets. In this case, researchers can apply to bring their research projects to the GSK facilities in Tres Cantos and draw on GSK’s drug discovery resources at no cost. An issue that is often not explicitly addressed in these initiatives is how priorities regarding R&D efforts are made. Although the actors that are involved in these partnerships and consortia share an interest in incentivizing further research on global health priorities, this research can be oriented to a multitude of outcomes and is not necessarily harnessed to the projects with the greatest likelihood to have an impact on global medical need.

A further step in the creation of pre-competitive spaces has been the implementation of ‘open source’ models, particularly in drug discovery. The Open Source Malaria initiative (OSM 52), for instance, applies open-source software to the hit-to-lead development of promising anti-malarial compounds. By making all the information publicly and immediately available open-source initiatives pre-empt the possibility of patents on the result of the collaboration, although they leave open the possibility of IP-protected projects further down the development pathway. In a similar spirit, MMV has created the “Malaria Box,” a collection of 400 compounds that the PDP makes available free-of-charge to any researcher in the world working on antimalarial drug discovery (22). Again, a condition for the use of the “Malaria Box” is to place in the public domain

50 GSK: GlaxoSmithKline plc (Pharmaceutical company based in Brentford, UK), http://www.gsk.com/
52 OSM: Open Source Malaria initiative, http://opensourcemalaria.org
all the data resulting from those compound screenings (within a period of 2 years). MMV is currently in the process of extending this initiative beyond malaria with the creation of the “Pathogen Box” (23). Many of these initiatives in “pre-competitive” or “open-source” innovation aim to remove the uncertainty of success inherent in the early stages of medical innovation.

At the global health level the needs for trust and clarity around the substance of a partnership is also at the country level and with international and national public authorities. A recent review, which focuses on emerging infections, cites several needs to enhance global collaborations through (24);

(i) Greater equity in access to technology and expertise and need for specific capacity strengthening activities
(ii) Barriers based around differences in commercial and academic drivers, including sharing of data
(iii) The need for bodies, to develop and share protocols, standards and arrangements and support resolution of conflicts of interest should they arise

The partnerships established further down the R&D pathway can be productive too. Establishing platforms for clinical research presents a new set of challenges that DNDi has addressed, as discussed above. The EU funded EDCTP is one of the best examples of how to organize North-South partnerships for the clinical evaluation of new health technologies. An important goal of this partnership is to facilitate R&D capacity-building in developing countries. So far EDCTP is so far has limited its activities to partnerships with sub-Saharan African countries. One of the most remarkable innovations that is effecting how teams work with patients and populations in clinical trials, surveillance and primary health care is mobile telephone technology. The rapid interaction with target populations, the collection and analysis of data at distance from patient or community, the way clinicians and researchers interact with patients and communities, is being changed so rapidly through m-health that the full implications for how collaborations and partnerships are established and work has still to be fully worked through (4).

New challenges have arisen as countries and international programmes aspire to the more ambitious targets of elimination and eradication of infectious diseases. These programmes often have political and economic endpoints in addition health outcomes. This requires an even higher level of agreement of strategy and objectives. A recent paper by Yang et al (2014), that discusses China’s drive to eliminate NIDs, emphasises the need to adopt “appropriate, integrated prevention and control measures that achieve cost-effective benefits in the control of disease burden” (25). Although a laudable target, those involved in public health understand that each point can be the subject of long discussion before agreement is reached.

Coalitions and networks are now key participants in this changing landscape, often having an emphasis on communication, shared vision, mutual support and research applications. With the considerable level of funding available and with many groups involved (see Section 2 above) that are often competing for the same funding, there is a greater need for umbrella groups that can provide, information, communication, integration and avoid duplication of effort and resource, and provide coherence to strategy. The BMGF initiated the alliance “United to combat NTDs”, following the London declaration, which acts as an umbrella organisation. As funding becomes tighter (11, 26), the need for harmonisation between sponsor and PDPs becomes greater. Several coalitions
were established by researchers in Europe and North America and are reaching out to scientists in DECs. African Network for Drugs and Diagnostics Innovation (ANDI 53) launched in 2008 as the first Africa owned and managed network is now well established and the model has since expanded to Asia and Africa (27).

4. The impact of successful Networks, Collaborations and Partnerships on global health and innovation

On Innovation and R&D

The success of PDPs and the growing participation of the private sector have made an impact in bringing forward new products (7). Many of these successes so far are “low-hanging-fruit” and discovery and development of novel products has proved difficult, costly and time consuming (especially the development of new chemical entities (NCEs) for treatment), with many of the problems previously confined to the pharma/biotech sector. New treatments for malaria, TB and NIDs are in clinical trials and most of the 138 product-related projects come from PDPs (11, 26). The development of novel vaccines, drugs and diagnostics has another dimension around ownership, investment, marketing and access (see below). The development of a business plan for NIDs by the ASEAN countries (16) and the full documentation of Regulatory requirements for drug development and clinical research in India are positive indicators for ownership and investment for this WHO South East Asia Region (SEARO) review (28). One additional area for attention is education and training. The awareness and expertise in translational research and medicine is normally, at the global level, based on experience and working on product development in the private sector, or occasionally in research institutes. There are now several courses available in this area in North American Universities, with few in other continents. Within the Southeast Asia region building a cohort of young scientists with the enthusiasm and flexibility to take on the challenges of translational research is essential for growth in the region. There are some initiatives, for example the Diploma on Research and Development of Products to meet public health needs organised jointly by Nagasaki University Japan and Thammasat University Thailand. The investments by governments into translational health institutes, for example the Translational Health Science and Technology Institute, New Dehli, Malaysian Institute for Pharmaceutical and Nutriceuticals, Penang, and Centre for Technological Development in Health (CDTS 54), Rio de Janeiro, might provide an opportunity to help to build this cohort.

One of the more contentious issues is IP, which is now at the centre of discussions about the future of global health, both in terms of how to incentivize more intense R&D efforts, and in relation to their impact to the affordability of new health technologies. Perhaps this is in itself the most significant change: that discussions about the role of IP are now frank and upfront, and involve a larger set of actors and stakeholders, not least a variety of global health advocates.

53 ANDI: African Network for Drugs and Diagnostics Innovation (PDP based in Abuja, Nigeria), http://www.andi-africa.org/
54 CDTS: Centre for Technological Development for Health (Portuguese: Centro de Desenvolvimento Tecnológico em Saúde), http://www.cdts.fiocruz.br/site/index.php
The evolving position of the BMGF on IP is a good marker of the changes in this field. Over the last few years the Foundation has developed a more proactive, more explicit approach to this issue, seeking to harness the power of IP to enhance global access to life-saving technologies, and to minimize the power of IP to de-incentivize innovation or restrict access. “Intellectual Property,” the Foundation states, “provides a great opportunity to think creatively and strategically about how we can reach our ultimate beneficiaries. The careful and deliberate management of IP (patents, copyrights, trademarks, trade secrets, and rights in data) and the associated rights created or accessed through foundation-funded projects is a critical component to achieving Global Access.” The Foundation now monitors closely the implications of prior or new IP on the future availability of the research and tools it sponsors.

This is just one of the many innovations in the use of IP to foster the discovery and implementation of new health technologies. Gauging the effect of these innovations requires that we attend to both ends of development pathway. That is, the ability of IP innovations to energize R&D activities, on the one hand, and their impact on the accessibility and affordability of the new medicines that will emerge out of the R&D process. While much of the discussion around IP and global health centres on the question of how to incentivize R&D in situations of perceived “market failure,” without an approach that links these research incentives to the ultimate affordability of new therapies we won’t be reversing the structural dynamics that currently limit the availability to life-saving medicines.

The WHO’s Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI) aims precisely at providing a comprehensive policy outlook on IP and global health, one that addresses both the need to incentive new R&D efforts and the requirements for makes the resulting health technologies affordable and accessible to the populations in need. The recently announced WHO Health R&D Demonstration Projects also purport to encompass these two dimensions of an IP strategy for public global health: the use of “open-knowledge” approaches to research and development coordination and the creation mechanisms to facilitate affordability. There are two alternative approaches to this double purpose: 1) to create partnerships that will extend a pre-competitive, not-for-profit model all the way through the development cycle of a new health technology, from early-stage R&D to final clinical evaluation and registration; or 2) to create mechanisms that would allow an effective de-linkage of R&D costs from the final market cost of a product, primarily by replacing traditional instruments of IP protection with an alternative system of rewards for successful innovative activity. It is important to note from the start that there is no one-size-fits-all approach to these questions. Assessments need to be made disease area by disease area, region by region, technical challenge by technical challenge. In what follows we review some of the existing tools to use IP innovations for the benefit of public health research, development and implementation.

The World Intellectual Property Rights Organization (WIPO) launched its WIPO Re:Search initiative.
Following the model of the patent pool, WIPO Re:Search is a platform that allows IP-holders to make proprietary resources available to researchers around the world who are working on neglected tropical diseases. An alternative course of action is to challenge the perception of IP tools by defining health technologies as “public goods”, thus limiting the reach of conventional private monopolies. Much depend, of course, on how the category of “public good” is defined. The WHO defines “public good” in a traditional economic way as “goods and services that are ‘non-rival’ and ‘non-excludable’”, and makes an interesting distinction between “final” public goods (e.g. eradication of polio) and “intermediate” public goods. While we have tools and policy instruments to promote the creation and protection of “intermediate” public goods, there has been less interest in formulating mechanisms for securing “final” public good.

On Innovation and Implementation

For the health technology to have its greatest impact, innovation in the process of implementation is essential (4). The technology itself is not enough to attain the ultimate goal of health equity, unless it is affordable, accessible and adoptable by those who need it the most. Problems and success stories associated with affordability were already discussed in the previous section using IP as an example. In this section, we will draw on some examples on changing people’s behavior through innovative interventions.

A Shang Ring (Wu Hu SNNDA Medical Treatment Appliance Technology Co., LTD ⁵⁹) is a cheap and easy-to-use product for male circumcision, which can painlessly remove the foreskin (29). Even with such a promising product and the approval from the FDA, its use in sub-Saharan Africa is limited to less than 5 % due merely to people’s resistance towards the product procedure. The lack of consideration of cultural resistance, even for a cost-effective product like Shang Ring, can sometimes cause a failure during the implementation process. However people can learn to accept a new technology. For example in Thailand, a community based HIV/AIDS intervention called the Mr.Condom campaign was effective in reducing 90% of the new HIV/AIDs infections during the first 12 years of the programme. This was done by raising awareness through rather controversial education programmes such as condom-blowing competitions at schools and peer education where university students taught the use of condom to secondary students (30). By focusing on individual to attain a good understanding about the need and use of a product made it possible to break the barrier of cultural resistance.

The use of behavioral economics during the implementation process, just like in consumer analysis, was also proven effective in Zimbabwe for its antenatal care programme (4). The intervention was successful in changing pregnant women’s subconscious behavior by providing a choice to opt-out from the free HIV-testing program. It is the human nature to avoid missing out on any possible

⁵⁹ Wu Hu SNNDA Medical Treatment Appliance Technology Co., LTD (Health technology company, based in Wu Hu City, China) http://snnda.en.alibaba.com/
benefits and thus the test coverage increased to over 90% during the first six months of the opt-out period in contrast to 65% of the opt-in period (4).

The evidence we currently have on the best practice of R&D product implementation is not yet sufficient. There is still a substantial need for researches to be conducted in order to understand more about how the process of health technology implementation can be improved at the global, national and individual levels. The complex strategies for behaviour change communication (BCC) are part of this process for intervention with individuals, communities and/or societies. They describe the development of communication strategies to promote positive behaviour that is appropriate to the settings with an aim to provide an environment that supports people to initiate and sustain positive and desirable behaviour outcomes.

Again, the need for education and training to develop a cohort of staff with awareness and expertise in programme development, evaluation (of process and programmes), BCC, and health system research is essential. Much of this is based on experience with Universities and Institutes in Europe and North America do provide specialist post-graduate training in many of these areas. In the SEARO region courses are in development, with Mahidol University Global Health Institute offering a full range of education options and PHFI (Dehli) offering a range of postgraduate courses, with both face-to-face and distant learning options, in health policy, health management and health informatics.
## List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ANDI</td>
<td>African Network for Drugs and Diagnostics Innovation</td>
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<tr>
<td>ASEAN – NDI</td>
<td>ASEAN Network for Drugs, Diagnostics, Vaccines and Traditional Medicines Innovation</td>
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<tr>
<td>ASEAN</td>
<td>Association of Southeast Asian Nations</td>
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<tr>
<td>BGMF</td>
<td>Bill &amp; Melinda Gates Foundation</td>
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<tr>
<td>CDTS</td>
<td>Centre for Technological Development for Health (Portuguese: Centro de Desenvolvimento Tecnológico em Saúde)</td>
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<td>CNS</td>
<td>Central Nervous System</td>
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<td>CPP</td>
<td>Certificate of a Pharmaceutical Product</td>
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<td>DAH</td>
<td>Development Assistant for Health</td>
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<td>DCCC</td>
<td>Developing Countries Coordinating Committee</td>
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<td>DECs</td>
<td>Disease Endemic Countries</td>
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<td>DNDi</td>
<td>Drugs for Neglected Diseases initiative</td>
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<td>DoPs</td>
<td>Diseases of Poverty</td>
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<td>EDCTP</td>
<td>European and Developing Countries Clinical Trials Platform</td>
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<td>EU</td>
<td>European Union</td>
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<td>FDA</td>
<td>US Food and Drug Administration</td>
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<td>GHIT</td>
<td>Global Health Innovative Technology Fund</td>
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<td>GSK</td>
<td>GlaxoSmithKline plc</td>
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<td>HAT</td>
<td>Human African trypanosomiasis Platform</td>
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<tr>
<td>HIV/AIDS</td>
<td>Human immunodeficiency virus infection and acquired immune deficiency syndrome</td>
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<td>ICMR</td>
<td>Indian Council for Medical Research</td>
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<td>IMI</td>
<td>Innovative Medicines Initiative</td>
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<td>IP</td>
<td>Intellectual Property</td>
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<td>IVCC</td>
<td>Vector Control, Saving Lives</td>
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<td>KEMRI</td>
<td>Kenya Medical Research Institute</td>
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<td>LEAP</td>
<td>Leishmaniasis East Africa Platform</td>
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<td>MDGs</td>
<td>Millennium Development Goals</td>
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<td>MMV</td>
<td>Medicines for Malaria Venture</td>
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<td>MPP</td>
<td>Medicines Patent Pool</td>
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<td>NCEs</td>
<td>New Chemical Entities</td>
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<td>ND4BB</td>
<td>New Drugs for bad bugs</td>
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<td>NID</td>
<td>Neglected Infectious Diseases</td>
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<td>NIH</td>
<td>National Institutes of Health</td>
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<td>NITD</td>
<td>Novartis Institute for Tropical Diseases</td>
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<td>Novartis</td>
<td>Novartis International AG</td>
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<tr>
<td>NTDs</td>
<td>Neglected Tropical Diseases</td>
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<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
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<tr>
<td>OSDD</td>
<td>Open Source Drug Discovery</td>
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<td>OSM</td>
<td>Open Source Malaria initiative</td>
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<td>PDP</td>
<td>Product and Development Partnerships</td>
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<td>PHFI</td>
<td>Public Health Foundation of India</td>
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Public Private Partnerships

Research and Development (R&D)

Single Exposure Chemoprotection (SEC)

Single Exposure Radical Cure and Prophylaxis (SERCaP)

Structural Genomics Consortium (SGC)

Diseases of the Developing World (DDW)

Tuberculosis (TB)

Target Product Profile (TPP)

United Nations Development Programme (UNDP)

WHO Special Programme for Research and Training in Tropical Diseases (WHO – TDR)

World Health Organization (WHO)

World Intellectual Property Rights Organization (WIPO)

References


Acknowledgements/Conflicts

SLC is an advisor to GSK, Novartis and the Wellcome Trust on drug R & D for neglected diseases
Developing a multidisciplinary approach for global health - clinical, epidemiological and basic research: A personal perspective by Gerald T. Keusch, M.D. Boston University, Boston MA.

Essential Elements for developing a multidisciplinary approach for global health

- Plan
- People
- Place
- Partners
- Parts
- Politics
- Persistence – and aligning all the P’s

The global health system\(^{60}\) is in a period of rapid transition, with an upsurge of funds and greater political recognition, a broader range of health challenges, many new actors, and the rules, norms and expectations that govern them in flux. The traditional actors on the global health stage—most notably national health ministries, the World Health Organization (WHO) and a relatively small group of national medical research agencies and foundations funding global health research—are now being joined (and sometimes challenged) by a variety of newer actors: civil society and nongovernmental organizations, private firms, and private philanthropists, and an ever-growing presence in the global health policy arena of low- and middle-income countries, such as Kenya, Mexico, Brazil, China, India, Thailand, and South Africa.

Framework for the GHS working group

“The ‘Acting in Time’ initiative launched in 2007 at the Harvard Kennedy School, grew from the observation that virtually all of the world’s most pressing problems, from climate change to health care to natural disasters to disease outbreaks to demographic change to terrorist threats, were relatively easy to see coming and would be far easier to deal with if peoples acted sooner rather than later. Yet in virtually every case, nations and institutions seemed unable or unwilling to act in time.”

Effective GHS have 5 core functions and their analysis resulted in following conclusions:

1. Agenda-setting: No single actor can or should set the agenda for action. Broad-based, participatory, transparent processes for agenda setting, anchored by WHO’s global political legitimacy and adhering to widely-accepted procedural principles, will be required to define priorities, avoid unnecessary duplication, and share knowledge.

2. Financing and resource allocation: Sustainability depends on strengthening national health systems. Donors should allow greater flexibility for recipient countries to direct a portion of received funds beyond narrow programmatic interventions to strengthening national health systems. Prioritize additional investments in longer-term, multi-disciplinary education and training.

3. Research and development: Support research that provides the evidence and knowledge

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bases for prioritization, resource allocation, the development and evaluation of new tools and interventions, and understand variation in the performance of different national health systems to identify critical features to adapt to local conditions. Basic and translational research and research capacity-building involving strong and long-term collaborations between technically advanced research institutions and emerging centers of excellence in disease endemic countries are essential.

4. Implementation and delivery: Ironically, the proliferation of global actors threatens to weaken health systems by placing additional reporting burdens on already thinly stretched health ministries. The global health system should identify and adopt analogous ways to streamline reporting and, more generally, to minimize the additional transaction costs put on countries.

5. Monitoring, evaluation, and learning: Systematic investment in new and improving existing M&E programs. Over time, this investment – if adequately financed – will contribute to building robust M&E systems and generate reliable, comparable data to inform action.

In order to prevent complexities to arise in health sector after an event has occurred. The principles of broad based agenda seeing, investment in national health (research) system, minimizing transaction costs, promoting long term collaborations, having in place systematic M&E programs, a multidisciplinary education and training system and policy decisions based in evidence.

**Principles to be followed in implementation of public health, innovation and IP aspects of GSPA**

- For individuals a combination of scientific training and mentoring from successful role models; creating a supportive environment among colleagues as nobody works alone; physician – scientists working with PhD/DSc/MS/MPH; linking biomedical engineering, computational and systems biology to healthcare environment; a full time career path in research with sufficient salary and scientists must be given opportunities to use their skills combined with sufficient salary to avoid diversions.
- For Institutions focus should be on labs, equipment’s, logistics for reagents and supplies; library, internet access to data bases, international connections (communication, conferences, courses); scientific ambiance – presentations, lab meetings, critical reviews, pilot funds, enlightened charismatic leadership from top, openness to inputs from below; grant preparation, management, financial audit; autonomy of investigator, especially junior faculty, including control of grant resources; ethics review system for human and animal research; functional system of grant support, review, decision making.

- It may be most effective to define the needs of the individual scientist first, and then create the supportive infrastructure required for success. Need information, analysis, assessment including external evaluations, flexibility, change
- Invest in the scientific pipeline of people – co-mingle disciplines beyond the health sciences. Ideal locus for this is the university
• Dangerous trends – corruption (falsification of data, plagiarism, skimming financial resources)
• Time line – long horizon vs short term; what is realistic, and what is sufficient to determine the quality of the work and its likely impact on innovation in R&D
• Consider the value of regional cooperation, how to complement skills and encourage participation. Need to overcome the inertia of political and cultural conflicts
• Connect academia to the private sector
• Technology transfer and IP expertise – betting correctly on what will be valuable. Clearly defined policy for royalty and licensing fees between institutions and investigators and their labs is a controlled incentive to innovate
• Innovation involves risk, risk means failures occur. How to manage innovational risks and failure in academic careers is a very tricky but necessary task
• Spinouts from academia to the private sector are essential and can be encouraged (or not), eg connections between the science enterprise and the business school
• When there are products to be made shortcuts may be taken by some for economic gain that threaten patient safety and product efficacy, a disaster for the whole system
• Availability of venture capital – typically investment driven
• Culture of philanthropy, or social venture capital – outcome (impact on target audience) driven


• Many institutions have multiple partners all of whom believe they are essential for institutional and individual scientist development. How do you assess the contributions of each? How do you assess the negative impacts of some? How do they interact with one another? It can be awkward to ask these questions, and doing so may be hazardous to continued support.
• Capacity building and its evaluation remains fragmented, essentially a project-by-project enterprise. Some funders may be more interested in how much corruption occurred than in how much leadership the local investigators assumed. Others may overlook the former if the latter outcome is favorable. There are multiple personalities involved, inter- with the collaborators as well as intra- within the institutional staff. How do you assess the functionality of these relationships?

Needs assessment by a local university for an international basic science training grant

• Existing training opportunities are rarely for basic science
• Time in an international setting is “essential”
• Sandwich model, with well-chosen candidates, options for post-doc training, ongoing mentoring, re-entry support
• Concern about the lack of critical mass at professorial level to support and mentor in basic sciences
• Adequacy of laboratory space, equipment, computers etc
• Optimally train “independent researchers, equip them with the tools to write grants, and they will go on to build the infrastructure”
• Enough high caliber local labs to provide opportunities for well trained scientists to return and build quality programs.
• Investing a lot in a few means ROI risk is high – essential to ensure appropriate positions are available so they return

The take-home trinity

• There is no free lunch – upfront investment funding is the mortar that holds the bricks together. This is a legitimate government role
• There is no time to waste – vision required and implementation critical
• Words are no substitute for action
INTRODUCTION

The World Health Organization (WHO) is working with Member States to implement the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI).

The GSPA-PHI is very broad in scope. It recommends specific actions across multiple sectors and at multiple levels (global, regional and national) to promote innovation in, and access to, essential medical technologies in low- and middle-income countries. While the WHO is working to implement the GSPA-PHI at all levels, the most important effort must be at the national level.

The strategy is based on specific actions that several stakeholders, mainly WHO and countries, should implement in various areas to ensure that capacity is developed to generate innovation in medical technologies, sufficient research is conducted to address needs of developing countries in terms of medical technologies and access to new, needed technologies is promoted in these countries.

As part of its efforts to implement the GSPA-PHI, the WHO has developed a National Assessment Tool (NAT) based on country-specific action items in the strategy. This tool facilitates a systematic assessment of the conducive environment to innovation for medical technologies, helping Member States to analyse their situation in terms of policies, regulations, legislations, infrastructure and funding. Furthermore, countries can benchmark their own strengths and weaknesses in implementing the GSPA-PHI and identify where policy interventions are needed. Specific actions to be undertaken at global and regional levels have been excluded, and specific actions that name the WHO as the key stakeholder have also been excluded unless those actions require information to be collected from countries, in which case a question has been formulated and included in this tool.

The development of this National Assessment Tool has benefitted from several recent complementary initiatives including: Strengthening Pharmaceutical Innovation in Africa,1 the Innovation Union Scoreboard,2 and the Draft HAI Africa Pilot Monitoring

Tool. Information collected through this tool will be retained in a web-based monitoring and evaluation platform developed by PHI as an integral part of the WHO's contribution to GSPA-PHI implementation (Element 8). This database will assist in:

- drafting GSPA-PHI country progress reports and reports to WHO governing bodies;
- tailoring WHO technical assistance to meet the needs of Member States; and
- identifying gaps and opportunities to be addressed by development partners.

STRUCTURE AND USE:

This National Assessment Tool takes the form of a semi-structured questionnaire. It is designed to guide the collection and assessment of all relevant information. However, low- and middle-income countries are so diverse that a one-size-fits-all approach is unlikely to succeed. This tool should be adapted as needed to fit each national context.

In general, the structure of this assessment tool follows the order of Elements in the GSPA-PHI. Similar questions have been grouped together under topics derived from Elements with one exception: references to traditional medicine in Elements 1, 3 and 5 have been formulated as questions and grouped together in a separate section.

At the end of each question in this assessment tool, relevant specific action items in the GSPA-PHI are noted. When such numbers are not provided, this means that while no specific action item is linked directly to the question the information is still required to complement or clarify other questions and complete the picture.

Responses to questions in this assessment tool are not expected in the form of "yes" or "no." In most cases, explanation and supportive documentation are required. WHO might already have collected some of the information requested by this questionnaire: in such cases, the information is provided and the respondent should either update it or confirm it. Those using this tool should be thoroughly briefed about its use. Regarding this last aspect, the WHO recommends the establishment of a National Task Force on implementation of GSPA-PHI comprised of relevant stakeholders from the public and private sectors including civil society organizations.

National Task Force: Members may include, but need not be limited to, representatives from ministries of health, science & technology, trade & industry and finance; national research councils and research institutions; the national regulatory authority; non-profit civil society organizations involved in health care delivery and economic development; trade associations and for-profit firms. Diverse membership will facilitate the collection

4 This platform ensures tracking of the implementation phase of the GSPA-PHI. It will provide member states with a tool to map their own efforts and serve as a repository for relevant documentation, a reporting tool to WHO governing bodies, a planning and coordination space for intersectoral policies, and a unique interface for health innovation issues. http://www.healthresearchweb.org/phi_beta
of accurate information needed by policy makers and development partners and to coordinate national effort in implementation of GSPA-PHI.
GSPA-PHI NATIONAL ASSESSMENT TOOL

NOTE ON "INNOVATION": The Global Forum for Health Research has defined “innovation” as “encompassing the entire process from the generation of new knowledge, to the transformation of that knowledge into useful products or services, to the implementation of those services or products.” For the purpose of this tool, “innovation” involves policies and practices that enable and encourage the development, production and delivery of existing and new drugs, vaccines, diagnostics and other medical devices to people who need them.

NOTE ON NATIONAL POLICIES/STRATEGIES: This tool contains questions about national policies or strategies in multiple sections including health research policy, S&T (or innovation) policy, ethical review policy, human resources for health policy, local public-private R&D partnerships policy, North-South technology transfer policy, trade and investment policy, industrial policy, anti-dumping policy, poverty reduction policy, medicines policy, and traditional medicines policy.

<table>
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<tr>
<th>PRELIMINARY QUESTIONS</th>
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<tbody>
<tr>
<td>1: Are you aware of any other assessments of your country’s health innovation capacity?</td>
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<tr>
<td>2: Does your country have a National Task Force on the GSPA-PHI?</td>
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## HEALTH RESEARCH AND DEVELOPMENT

### Health R&D Policies and Infrastructure

1. **National strategy(ies) and priority setting:** Does your country have a national health research policy or strategy? If yes, please comment on the strategy’s goals and describe the mechanisms for intra-ministerial coordination. Please provide links to sources of information.

2. **Domestic support and leadership:** Does your country have a national health research council or equivalent domestic funding body/agency? What is its structure? Please provide links to sources of information.

3. **Research institutions, capacity and accreditation:** What are the key publicly-funded R&D centres/institutes in your country? (Element 3.1.b) What is the balance of publicly-funded research taking place in universities, government research institutions, hospitals, field sites and non-governmental organizations? Does your country have systems to accredit universities, courses and other training, including research training? Please list WHO collaborating centres in your country, and provide links to sources of information.

4. **Priority setting:** Has your country established needs-based priorities for health R&D? What was the process for their definition (e.g. did it include relevant stakeholders)? How often are these priorities reassessed? (Element 1.2.a) Has your country included health system research in the national health research policy/strategy or in any other equivalent document? (Element 1.2.c) Please provide links to sources of information.

5. **Research networks:** Do researchers and/or research institutions in your country participate in national, regional and/or global health research networks or groups? (Element 3.1b) Please provide links to sources of information.

### Funding for Health R&D

6. **Public spending:** What is the national health budget? What is the public budget for health R&D? How much does the private sector spend on health R&D? (Element

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5 e.g., (i) permanent/semi-permanent network such as academic societies/associations or ad hoc/time-limited joint venture for a specific research project; (ii) network/group to be composed only of public sector institutes, only private sector institutes, or both public and private sector institutes, etc.

6 Total government health expenditure, total health expenditures as % of nominal GDP, government health expenditure as % of total government expenditure
1.2e) If possible, provide trends in such funding over the past 5-10 years. (Element 1.2e) [POSSIBLE SOURCE: National Health Accounts]

7. External support: Provide information related to donor funding for public sector health research programs including health-related innovation. (Element 2.1.b,c)

8. Tracking and transparency: Does your country have publicly accessible information on sources of financing for health R&D? If yes, please provide details.

### Discovery Science and Clinical Research

9. Clinical trials capacity: Are there any public and/or private efforts in your country to build capacity to conduct clinical trials? Does your country maintain a publically available clinical trials registry? Please provide a brief description of clinical trials capacity in your country, both public and private (e.g., contract research organizations), as well as links to sources of information.

10. Ethical review: Is there a national ethical review policy for clinical trials? Does it cover the composition and functions of institutional ethical review committees? Where have such committees been established, and are they linked to other similar committees through national, regional and/or global networks? (Elements 2.2.f, 3.3.b, 3.3.c) Please provide links to sources of information.

11. International collaboration: Does your country participate in international efforts to build capacity and improve information in this area, e.g., International Clinical Trials Registry Platform (ICTRP) or European and Developing Countries Clinical Trials Partnership (EDCTP)? (Elements 2.2.f, 3.3.b, 3.3.c, 6.2.f)

### Access to Knowledge

12. Scientific literature: Does your country make available public health literature in local languages for health researchers in national academic and government research institutions?

13. Compound libraries: Does your country maintain compound libraries? (Element 2.2.a,b) If yes, please provide a list, description, and note whether your country provides open access to these. Do researchers in your country have access to compound libraries established abroad? Please provide details. (Element 2.2.a,b)

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8 Definition of compound libraries from Nature.com: A structurally diverse collection of chemical molecules, typically containing several hundred thousand entities, that is used to identify new lead candidates. [http://www.nature.com/nrg/journal/v5/n4/glossary/nrg1317_glossary.html](http://www.nature.com/nrg/journal/v5/n4/glossary/nrg1317_glossary.html)
14. Relevance to product development: If such open-access is available (as explained above), has it led to any new medical products? (Element 2.2.a)

BUILDING AND IMPROVING INNOVATIVE CAPACITY

Human Resource Needs

15. National policy: Does your country have a national policy or strategy focusing on human resources for health? If yes, does this policy include health researchers? Does it include incentives to retain health professionals including researchers? Please provide details. (Element 3.2.b,c)

16. Public investment: How much does your country invest in education and training of researchers and public health workers? (Element 3.1.a)

17. Future workforce, general: What disciplines are taught at university level related to public health, health research and health innovation? How many doctoral students per discipline does your country have? What has been the trend over the last 5-10 years? (Element 3.1.a) Please provide links to sources of information. [POSSIBLE SOURCE: UNESCO]

18. Local production: Do universities in your country provide education in industrial pharmacy, technology assessment, technology management, business management and entrepreneurship, project management and accounting? Do they have basic and applied tertiary science education and research training relevant to drug manufacture (e.g., medicinal chemistry, pharmacology, biostatistics, target identification, etc.) and vaccine manufacture (e.g., antigen development, vaccine formulation and industrial engineering education covering biologics manufacturing)? Please provide links to sources of information.

19. IP management: Has there been any assessment of education and training needs for IP management, drafting and negotiating licenses, drafting patent applications, patent management, claims interpretation, how to manage IP “creatively” to promote both innovation and access, how to use TRIPS flexibilities and how to draft IP-related legislation that is sensitive to public health needs? (Element 5.1.a,e) Please provide links to sources of information.

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9 Medicine, pharmaceutical science, health economics, traditional medicine, nursing schools etc.
10 Life sciences, pharmaceutical sciences, chemistry, biology, traditional medicine, biotechnology, genomics etc. Please, refer to doctorate candidates with the nationality of your country that graduate from local
20. Dialogue with industry: Do educational institutions and the education ministry in your country have mechanisms for continuing dialogue with representatives from industry to match curricula with industry needs? If yes, please provide details.

Incentives for Health Innovation

21. “Putting fuel in the tank” (rewarding academics): Is there a policy or mechanism in your country to encourage health researchers to contribute to technological innovation (e.g., career advancement linked to patenting and/or industry collaboration)? \(^{11}\) (Element 3.5b) Describe these mechanisms.

22. “Engaging the gears” (local public-private R&D partnerships): Does your country have national policies to encourage R&D partnerships between publicly funded research institutions and local industry (e.g., Bayh-Dole-like legislation)? Please list examples of such partnerships, if any, and describe outcomes. Do academic and government research institutions in your country have Technology Transfer Offices (TTOs) to facilitate such partnerships to translate publicly funded research knowledge into products? If so, have they developed institutional policies to encourage access to inventions that arise from public investments? \(^ {12}\) Please provide links to sources of information.

23. “Driving innovation” (with push and pull incentives): What incentives exist in your country to encourage and reward local entrepreneurs and manufacturers in order to strengthen local innovation and production of health products (Element 3.5.a)? Examples may include R&D grants, tax breaks for R&D, business incubators, recognition and/or monetary prizes, soft-loans, preferential pricing for procurement from local manufacturers, restrictions on importation, grants to local public-private R&D partnerships and for Small Business Innovation Research (SBIR) to help local industry attract private capital and encourage the creation of spin-off companies from academic and government research institutions. Please distinguish between domestic incentives and those (if any) from external development partners. Please provide sources and examples.

24. “Steering” innovation toward affordability and access: Are any such incentives specifically designed to promote affordability and access for medicines that are a high priority to the national health system? Please provide sources and examples.

25. Understanding national health information system: Provide details about national health surveillance and information systems (Element 3.1c). Are there any assessment reports on the national health information system of your country?

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\(^ {11}\) In public or private academic institutions or government laboratories.

\(^ {12}\) For example, have they signed the AUTM Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies?
26. Partnering: Are there any North–South and/or South–South partnerships and programs for capacity building in the area of health innovation? (Elements 3.3.b, 2.2.f, 4.2.a) Please provide links to sources of information.

MANUFACTURING OF PHARMACEUTICALS

NOTE: Questions 26-30 are drawn primarily from GSPA-PHI Element 4, Questions 31-50 are based on legislative and industry sections of "Strengthening Pharmaceutical Innovation in Africa," a project of the New Partnership for Africa’s Development (NEPAD) and the Council on Health Research for Development (COHRED).

International Transfer of Technology

27. National strategy: Is there a national strategy or policy to encourage and assist local manufacturers to acquire technologies from other countries for local production of health care products (“North-South” technology transfer)? Please provide links to sources of information.

28. Technology assessment: Is there a capacity for technology assessment in your country? Is there any recent assessment of technologies needed for health R&D and for local production of health products? (Element 4.3.b) Please provide links to sources of information. (See Q: 20, 43)

29. Tracking collaboration and outcomes: Does your country have a system for recording initiatives to facilitate technology transfer for local production of health products including: national, South-South and North-South cooperation? (Element 4.2.b) Does your country measure the contribution of local production to access to health products? Please provide links to sources of information.

30. Case studies: Does your country have examples of success stories or failures in North–South and South–South technology transfer for local production of health products? Please provide links to sources of information. (Elements 4.2.a, 3.3.b, 2.2.f)

31. External private investment: What is the level of foreign private investment (FDI and other financial flows) in pharmaceutical and other essential health technologies in your country? Please provide links to sources of information.

13 This covers medicines, diagnostics, vaccines medical equipment and other medical devises…
Local Production: Policies, Capacity and Legislation

32. National policies: Does your country have a national trade and investment policy? Does that policy cover active pharmaceutical ingredients (APIs) and biologics? Does your country have a national industrial policy? Does it cover the biotechnology and pharmaceuticals sectors? Does your country have a national science and technology (or innovation) policy or strategy? Does it include the health sector? Does it balance economic aspirations with improvements in well-being, including public health? What mechanisms are in place for intra-ministerial coordination of the S&T/innovation policy? Please provide links to sources of information.

33. Publicly funded research institution capacities: Are academic and government research institutions in your country able to act as sponsors for clinical trials? Do they have facilities (e.g., animal facilities) and the technical capacity to meet international licensure standards (Good Laboratory Practice) for drug discovery and for preclinical studies including preclinical vaccine studies (e.g., toxicity)? Do they have access to vaccine delivery systems and adjuvants? Please provide links to sources of information.

34. Biosafety: Do biosafety facilities exist?

35. Border controls: Does your country minimize tariffs and duties on imported APIs? Describe. Can customs controls distinguish genuine from counterfeit API imports and exports? Does your country have anti-dumping policies (e.g., punitive tariffs)? Please provide links to relevant sources of information.

Industry Capacity for Local Production of Existing Products

36. Good Manufacturing Practice: Are pharmaceutical firms able to comply with Good Manufacturing Practice (GMP) in the manufacture of health products? Please provide links to sources of information.

37. Importing Active Pharmaceutical Ingredients (APIs): Are pharmaceutical firms able to identify API certified suppliers and test identity, quality and safety of procured APIs? Are they able to specify and test API requirements, e.g., formulation design, which can affect stability and bioavailability of finished drugs? Are they able to conduct bioequivalence studies of generic formulations? Please provide links to sources of information.

14 "Dumping" happens when a manufacturer offers its product(s) at a price or quantity that cannot be explained through normal market competition. This may force other manufacturers out of a market, or completely out of business, leaving the "dumper" with a monopoly position. (http://en.wikipedia.org/wiki/Dumping_(pricing_policy)
38. Manufacturing and distributing generic drugs: Are pharmaceutical firms able to undertake formulation, process and scale-up of generic drugs? Are they able to produce APIs to GMP standards and pharmacopoeia requirements? Are they able to undertake small to large-scale manufacturing, commercialize appropriately for local markets and link to local distribution networks?

39. Vaccine production: Do firms have facilities specifically tailored to undertake large scale GMP-standard vaccine production (e.g., sealed fermentation, aseptic production and purification, and large-scale harvesting)?

40. Vaccine quality control and assurance: Are vaccine producers able to maintain and demonstrate a completely controlled production process (i.e., carry out stability and potency studies; maintain potency and yield during sterile filtration of particle-containing solutions; carry out full tracking of manufacturing batches and lot-by-lot release of vaccines)? Do firms have dedicated in-house quality control laboratories for assay development and processing?

41. Meeting regulatory requirements: Are pharmaceutical firms able to prepare drug master files for registration with the National Regulatory Authority? Are they able to prepare regulatory dossiers for generic drug registration, using both data from their own studies and referencing quality, safety and efficacy data from original drug regulatory files?

Industry Capacity to Develop New Products

42. Improving known products: Are public and/or private sector manufacturers able to access rights to original drugs and registration data for further development (e.g., combination therapies and new formulations)?

43. Preclinical testing: Are public and/or private sector manufacturers able to conduct drug and/or vaccine discovery and preclinical studies, bioequivalence studies and complex drug and vaccine clinical trials to international licensure standards? Are they able to access compound libraries and screening facilities? Are they able to access adjuvants and vaccine delivery technologies, and to conduct feasibility studies for large scale vaccine manufacturing?

44. Meeting regulatory requirements for new products: Are public and/or private sector manufacturers able to prepare regulatory dossiers for clinical trial authorization and drug and biologics (vaccine) registration using data from their own clinical studies and referencing quality, safety and efficacy data from original drug regulatory files?
45. Clinical trials: Are public and/or private sector manufacturers able to design and implement clinical development plans for drugs and biologics (vaccines), and to sponsor drug and vaccine trials?

**APPLICATION AND MANAGEMENT OF INTELLECTUAL PROPERTY**

**Trade Agreements and Intellectual Property (IP)**

46. WTO, WIPO and TRIPS flexibilities: Is your country a member of the World Trade Organization (WTO)? Is your country a member of the World Intellectual Property Organization (WIPO)? Does national patent legislation incorporate flexibilities available under TRIPS? If yes, which ones? Please provide link to relevant legislation.

47. Regional and bilateral agreements: Is your country a member of a relevant regional organization? Has your country entered into bilateral or regional trade agreements which have resulted in IP protection going beyond what is required by the TRIPS agreement? Does your national legislation go beyond what is required by the WTO TRIPS agreement with respect to pharmaceutical products? Do health representatives in your country participate in bilateral and multilateral trade and IP negotiations? (Element 5.1.g) Please provide links to sources of information.

48. Assessment of IP legislation: Has there been any assessment of national IP legislation with regard to public health? (Elements 5.2.a,c,d, 6.3.a) Please provide links to sources of information.

49. Intra-ministerial coordination: What mechanism does your country use to coordinate policies on public health, intellectual property and trade? (Element 5.1.h) Please provide links to sources of information.

50. National patent office: Does your country have a national patent office? Does your country maintain a national database on patent applications and patents’ legal status (patent registry) and is it available online? Please provide links to sources of information.

51. Protection of data disclosed to regulatory authorities: Does your country provide for protection of clinical test data submitted to the national regulatory authority (as required by TRIPS to prevent unfair commercial use)? If yes, how? Please provide links to sources of information.

52. Research exemption: Does legislation in your country provide a research exemption to ensure that research involving patented inventions is not considered infringement? (Element 2.4.e) Please provide links to sources of information.
IMPROVING DELIVERY AND ACCESS

Access to Quality Medicines

53. Policies: Is there a national poverty reduction strategy in your country, and does it address the health sector? (Element 6.1.f, 6.3.b) Is there a national medicines policy in the country, and a national essential medicines list? Does the national medicines policy include improving access to affordable medicines as one of its objectives? (Element 6.3.b, 6.1.f) Please provide links to sources of information.

54. Product quality: Are any of the following standards/guidelines available in your country: Good Manufacturing Practices (Element 6.2.c); Good Clinical Practice (Elements 2.2.f, 3.3.b, 3.3.c, 6.2.f); and Good Laboratory Practice? Is there a national quality control laboratory in your country? Are any medical products from your country prequalified by the WHO? (Element 6.2.d) If yes, please list them.

Delivery Infrastructure and Incentives

55. Procurement mechanisms: What is the per-capita expenditure on medicines by government in your country, and what have been the trends over the past 5-10 years? (Element 6.1.a) Is your country part of any pooled procurement program for health products? (Element 6.1.g) If yes, please list them.

56. Delivery infrastructure: What are the strengths and weaknesses in the health delivery infrastructure in your country? Has there been any formal assessment of this infrastructure? (Element 6.1.a) Please provide links to relevant sources of information.

57. Local incentives for delivery innovation: What mechanisms are in place to create incentives for local delivery innovation, and for the adoption and adaptation of cost-effective health product and service delivery approaches from other countries or other sociocultural contexts?

Regulation of Safety and Efficacy

58. Regulatory framework: Are legal provisions that establish the functions and responsibilities of the national regulatory authority in place? Does the NRA have a website? Does the NRA participate in harmonization or collaboration initiatives? Does the NRA use an electronic information management system to keep and

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15 Refer to WHO assessments
### Marketing authorization (licensing)

59. Marketing authorization (licensing): Does the NRA have a legal provision that requires a marketing authorization (registration) for all pharmaceutical products on the market? Are there legal provisions that require the NRA to make publicly available registered pharmaceutical products with defined periodicity? Are there legal provisions requiring the NMRA to publish the Summary Product Characteristics (SPCs) of the pharmaceuticals registered? If yes, please provide link to relevant legislation (or provide article number).

### Inspections

60. Inspections: Are there legal provisions that exist permitting inspectors to inspect premises where pharmaceutical activities are performed? Are there legal provisions that require manufacturers to implement adequate GMPs? If yes, please provide link to relevant legislation (or provide article number).

### Import controls and licensing

61. Import controls and licensing: Are there legal provisions that exist requiring authorization to import medicines? Are there legal provisions that exist allowing the sampling of imported products for testing? Are there legal provisions that exist requiring manufacturers to be licensed?

### Market control and quality control

62. Market control and quality control: Are there legal provisions for quality control of the pharmaceutical market? Does a national laboratory exist in the country for quality control testing? If yes, please provide link to relevant legislation (or provide article number).

### Clinical trials

63. Clinical trials: Are there legal provisions that exist requiring NRA authorization for conducting clinical trials? Are there legal provisions that exist requiring the agreement by an ethics committee/institutional review board of the clinical trial to be performed? Are there legal provisions requiring the sponsor and investigator to comply with Good Clinical Practices (GCP)? If yes, please provide link to relevant legislation (or provide article number).

### Pharmacovigilance

64. Pharmacovigilance: Are there legal provisions that provide for pharmacovigilance activities as part of the NMRA mandate? Does a national Adverse Drug Reactions database exist in the country? Does a routine and crisis communication strategy exist? If yes, please provide link to relevant legislation (or provide article number).

### Capacity and practice

65. Capacity and practice: What are the staff numbers, budget and other capacity measures for the national regulatory authority (NRA) of your country? Is there any formal assessment report available on the NRA? Does the NRA regulate clinical trials? If so, does it require that all clinical trial data must be obtained from ethically approved trials? (Elements 3.2.a, 6.2.a)
66. Harmonization or creation of regional authorities: Is your country’s NRA part of any regional or sub-regional regulatory harmonization program? (Element 6.2.e) Is your country involved in negotiations that could lead to the creation of a regional regulatory authority to improve economies of scale, transparency and governance?

**Affordability of Medical Products**

67. Promoting generics: Are users, doctors and pharmacies in your country encouraged to use generic medicines. (Element 6.3.g) Please provide details. Does the national patent law in your country have a regulatory exception (“Bolar” type provision) by which generic versions can be introduced immediately after the expiration of a patent? (Element 6.3.a, 5.2.a,c,d)

68. Understanding costs: Has there been any medicine price survey in your country? Is there a price monitoring mechanism? (Element 6.3.e) Has any study been conducted to understand different price components (e.g., tariffs, whole-sale and retail-sale margins, etc.)? Does the government impose import duties on raw materials and finished products? (Element 6.3.c) Please provide links to sources of information.

**PROMOTING SUSTAINABLE FINANCING MECHANISMS**

**Public-Private R&D Partnerships (PDPs)**

69. Global PDPs: Is your country involved in partnerships with any global public-private product development partnership (PDP; e.g., International AIDS Vaccine Initiative, Medicines for Malaria Venture, Global Alliance for TB Drug Development, DNDi)? (Element 7.2a) If yes, please provide details on the partnership(s).

70. Domestic support for global PDPs: Does your country give either financial or in-kind support to global PDPs? Please, provide details. (Element 7.2c) Does your country periodically assess the performance of local collaboration with global PDPs? If yes, please provide details and methodology. (Element 7.2b)

**New sources of funding**


Consultative Expert Working Group on R&D Financing, for revenue generation to support domestic health innovation?
TRADITIONAL MEDICINE

Health, health research and health innovation policies

72. National policies: Does your country have a national policy on traditional medicine? If yes, does it cover issues related to innovation in the field of traditional medicine? (Element 3.4 a.b,c) Has your country included traditional medicine in its national health R&D strategy, and are there any R&D priorities identified in traditional medicine? (Element 1.3.a) Please provide links to sources of information.

Production, Regulation and Protection

73. Production and development: Is there any local production of traditional medicines in your country? If yes, do publicly funded research institutions and/or private manufacturers have an ability to systematically evaluate and screen traditional medicines for successful compounds to be identified, developed and marketed?

74. Regulation: What is the status of regulation of traditional medicine in the country? Are there any national standards for quality production and R&D for tradition medicine? (Element 3.4.c) Please provide links to sources of information.

75. Protection of traditional knowledge: What mechanism does your country use to prevent the misappropriation of traditional (medicinal) knowledge? Are there digital libraries for traditional medical knowledge, and do patent examiners have access to such information when examining patent applications? (Element 5.1.f.e) Please provide links to sources of information.

MONITORING AND REPORTING

76. Health metrics and health information system: How are health and health system-related data and information collected in your country? In what form are such data and information available? Are there any on-going or planned national surveys on health-related issues in your country? Does your country participate in international initiatives to monitor progress in achieving the Millennium Development Goals? If yes, please list them.

17 i.e.: clinical trials, epidemiology data (burden of diseases), medical records, healthcare facility and hospital management data, human resources for health.
77. Domestic M&E profession: Does your country have professional associations or organizations of experts in monitoring and evaluation (M&E) in the social sector? If yes, please provide a list.
Review of Canada’s Key Contributions to Global Health Research and Innovation by Halla Thorsteinsdóttir

Introduction

The dialogue on global health research has been increasing in Canada, as in many other high-income countries, over the last few decades. In 2002, one of Canada’s key funders of health research, the Canadian Institutes for Health Research (CIHR), declared that global health research was one of its five major strategic initiatives. [1] Since then, several initiatives have been set up that focus on different aspects of global health research and innovation. This paper reviews Canada’s key contributions to global health research and innovation as an input to the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property. The paper maps Canada’s emphasis on global health research and compares it to other global contributors. It then introduces Canada’s key global health funders, discuss the main features of Canadian research in global health and its contribution to innovation.

The paper follows a broad definition of global health developed by Koplan et al (2009) that emphasizes its interdisciplinarity. According to their definition, global health is:

“...an area for study, research, and practice that places a priority on improving health and achieving equity in health for all people worldwide. Global health emphasizes transnational health issues, determinants, and solutions; involves many disciplines within and beyond the health sciences and promotes interdisciplinary collaboration; and is a synthesis of population-based prevention with individual-level clinical care.” [2]

What follows will, therefore, discuss global health research that focuses both on health systems and policies, and on developing new health products and services. The focus in this paper will be on the global health issues of populations in low- and middle-income countries, rather than those of the Canadian population.

Mapping Canada’s efforts in global health research and development

Key research areas

Canada’s strength in global health research is not a widely researched topic. In recent years there have been some efforts to identify those areas of global health research Canada has emphasized. Gabriel et al (2010) examined, for example, CIHR’s financial contribution to the research of the 13 most prevalent neglected tropical diseases (NTDs). In total, between 1999 to 2009, CIHR allocated C$29.8 million to study NTDs, representing 0.46% of CIHR’s research budget. The study further showed that most Canadian funding went for Leismaniasis research, which received 70% of funding for NTDs [1]. Other diseases of considerable emphasis were Trachoma, Leprosy and Chagas disease. In comparison, HIV/AIDS received 3.99% of the funds, tuberculosis 0.56%, and malaria 0.22%. It is also important to note that that there was no increase in CIHR’s funding for NTDs between 2001 to 2009.

Considering the funding emphasis on Leismaniasis, it is not surprising that Phillips et al (2012) identified that Canadian authors had, from 1950 to 2010, published most papers on Leishmaniasis (423 papers or 40% of Canada’s NTD publications), followed by African Sleeping Sickness (186 papers) and Leprosy (148 papers) [3]. Their research showed that there was a steady increase in publications on NTDs from 1981 to 2010.

To better understand Canada’s standing in knowledge production on Leishmaniasis, we looked at the numbers of research articles published by authors with addresses in Canada listed in the Scopus
From 2010 to 2013, Canada was in 11th place in terms of total numbers published on Leishmaniasis, behind European countries such as Spain, Italy and Belgium. Thus, despite an emphasis on Leishmaniasis research, Canada’s knowledge production in this field is only average, if measured by the quantity of papers published by Canada on this disease. Other measurements of Canada’s role in this research area could include measurements of the influence of the papers in the global community with a citation analysis, but that is beyond the scope of this paper.

Another emerging area of global health is research on the Ebola virus. Here, Canada’s global standing is much stronger than in Leishmaniasis research. From 2009 to 2013, Canada placed second globally in terms of number of research articles on Ebola. As in many health fields, the United States is by far the largest producer of research on Ebola, but Canada is ahead of countries such as Germany, Japan and the United Kingdom.

Canadian researchers, thus, seem to publish papers on a number of global health themes. Their standing compared to other knowledge producers in the world seems, however, to differ depending on the disease focus. As will be discussed further below, Canadian researchers focus on much more varied health needs in developing countries than NTDs, but there is so far limited research that examines the extent of Canada’s global health research.

**Key funders**

What are known as the G-Finder reports annually trace financial information on research and development efforts for neglected diseases. The latest report presents Canada’s public funding from 2007 to 2012 compared to other main public funders of neglected diseases [4]. While Canada makes it on the list of top 12 public funders of research and developmental activities on neglected diseases, it is in the 10th place and the extent of Canada’s funding is lower than funding from countries such as Australia. Further, 2012 was the only year when Canada allocated a comparable amount to neglected diseases as Sweden, a much less populous country. According to the report, some of the changes between years for Canada’s contribution to research and development of neglected diseases is due to improved reporting. There may still be scope for Canada to improve its reporting on this topic and thus the contribution could be underestimated.

The funding reported in the G-Finder report is, for the most part, allocated by CIHR. There are other public funders of global health research in Canada that have a wider global health focus, beyond only neglected diseases. Canada’s International Development Research Centre (IDRC) has had a long-standing focus on health and health care delivery as priority areas, and places a relatively strong emphasis on research on health policies and health systems [5]. Research on global health systems is an area that Canada has some strengths in and Canada was, for example, number three in the world in terms of number of publications on health systems from 1900-2012 [6]. IDRC now includes programs in Ecosystems and Human Health; Governance, Equity and Health; and Non-Communicable Disease Prevention. In 2001, together with CIHR, the Canadian International Development Agency (CIDA), and Health Canada, IDRC and the Public Health Agency of Canada established the Global Health Research Initiative, and is its host [7, 8]. At present, the agencies active in this initiative, apart from IDRC, are CIHR and Foreign Affairs, Trade and Development Canada (DFATD). Its key focus areas are the following:

- prevention and control of pandemics and emerging infectious diseases
- prevention and management of chronic diseases
- health policies and systems
- interactions between health, the environment, and development [9]

Since it was established, 125 initiatives have been managed under the auspices of the Global Health
Another Canadian public initiative aimed at fostering global health research is Grand Challenges Canada. It is a non-profit organization and was established in 2008 to implement and manage projects supported by the Canadian Federal Government’s Development Innovation Fund. Grand Challenges Canada’s work is overseen by IDRC and CIHR. Grand Challenges Canada’s original vision was to harness “technological, business and social innovation in Canada and in low- and middle-income countries to save and improve lives” [10]. In its most recent annual report, Grand Challenges Canada reported that it had signed agreements for CAD $148 million to fund 538 projects, to be carried out in more than 70 countries [10]. The organization has leveraged a total of CAD $189.8 million in additional funding, including substantial private sector contributions. Its projects span a wide spectrum of areas. It has a ‘Stars in Global Health’ program that has a broad focus on the use of scientific/technical, social and business innovation to address health challenges in diverse global health areas. Grand Challenges Canada also has more specific programs that target the challenges of women’s and children’s survival, child development and global mental health.

In addition to the initiatives discussed above, Canada also actively takes part in international initiatives in global health. CIHR, for example, partners with other health funders in the Global Alliance for Chronic Diseases. There are also independent non-governmental organizations in Canada supporting global health research. For example, the Canadian Coalition for Global Health Research aims to increase and advance knowledge of health systems, human health and the conditions that contribute to human health [11].

From the discussion above it is clear Canada actively promotes global health through a number of different initiatives. The themes of global health that Canada promotes span a wide range, from neglected tropical diseases, to chronic diseases, maternal health and mental health. Canada also promotes global health research on health systems, and policy. The research that Canada supports is either carried out by Canadian researchers or by researchers in low- and middle-income countries. IDRC, for example, is heavily focused on supporting research carried out in developing countries. It does not report separate statistics on its support of global health research, but its total projects are predominantly carried out in developing countries, with only 15% of them involving Canadian researchers [12]. Grand Challenges Canada is also aimed at research carried out in developing countries, with 321 institutions in 40 developing countries involved in its activities and 196 institutions in Canada [10]. It is also involved in implementation of research as will be discussed below.

Mapping Canada’s global health research efforts, therefore, shows that there has been considerable spread of those efforts in various developing countries. This diversity in global health themes and locations that Canada promotes is not captured well by the G-finder reports discussed above. The global health themes covered by Canadian funders seems to be wider than those included in the report, and their reporting of Canadian efforts appears to be incomplete.

The main features of Canadian initiatives in global research and development

This section will discuss some key features of Canada’s global health research, including a discussion on how research areas are prioritized; the emphasis on capacity building; and supporting cooperation and networks.

Prioritization of research areas
Examining the main programs that Canada supports, the strong influence of the Federal Government’s prioritization of global health is apparent in the choice of research areas. At the 2010 G-8 meeting in Muskoka, Canada, Canada’s Prime Minister Stephen Harper announced the country’s commitment to allocate CAD $1.1 billion for Maternal, Newborn and Child Health [13]. This was in addition to CAD $1.75 billion in continued baseline funding, resulting in Canada’s committing to spend a total of CAD $2.85 billion on maternal and child health.

Canada also encouraged contributions from other G-8 countries and funders, such as the Bill & Melinda Gates Foundation, leading to the total commitment as a part of the Muskoka Initiative reaching US $7.3 billion. The Muskoka Initiative is said to result from advocacy efforts from global health experts and advocates during the mid-2000s that called for actions to promote maternal and child health [14]. Improving maternal health and reducing child mortality were also Millennium Development Goals advocated by the United Nations [15]. The Muskoka Initiative considerably increased Canada’s development assistance towards health. As a result, Canada was ranked as the fifth largest development donor for health in 2011, just behind the United States, the Bill & Melinda Gates Foundation, the United Kingdom, and the World Bank [14].

In light of the emphasis placed on maternal and child health by the Canadian government, it is not surprising that Canadian funders such as IDRC and Grand Challenges Canada follow this lead and emphasize these themes in their promotion of global health research. According to the IDRC Strategic Framework for 2010-2015, “program choices will be congruent with the priorities of Canada’s international development, innovation, and science and technology (S&T) agendas.” [16]. The GHRI has, for example, established the Innovating for Maternal and Child Health in Africa program and allocated CAD$ 36 million for its operation [9]. Grand Challenges Canada has established initiatives such as ‘Saving Lives at Birth’ and ‘Saving Brains’ which focus on child development and health, and also supports maternal and child health in its other programs, with 35% of its ‘Stars in Global Health’ program having so far been allocated, through peer review, to maternal, newborn and child health. In total, about half of Grand Challenges Canada’s work is focused on maternal and child health [10].

IDRC has also emphasized that it responds to locally defined research priorities and needs when prioritizing its work in general [16]. To determine these, it carries out consultations broadly with its partners and with diverse stakeholders, and the results of these consultations inform its strategic planning. Details are, however, scant in publicly-available documents on how these consultations are carried out.

Grand Challenges Canada states that its prioritization of research themes is based on the grand challenges in global health approach. According to this approach, a grand challenge is:

“One or more specific critical barrier(s) that, if removed, would help solve an important health problem in the developing world with a high likelihood of global impact through widespread implementation.” [17]

In 2003, the Bill & Melinda Gates Foundation supported a systematic approach to identify 14 grand challenges in global health [17]. Coalitions of global health experts have also identified grand challenges in chronic non-communicable diseases and in mental health [18, 19]. According to Grand Challenges Canada, over 50 individual global health challenges have been identified in the past decade. These challenges direct its work, and the organization uses the following criteria to flesh out broad thematic areas and specific challenges within these themes:

1. Burden of diseases
2. Tractability
3. Impact
4. Integrated innovation
5. Current funding landscape
6. Canadian expertise
7. Branding and niche
8. Potential topics [17].

Details are, however, lacking in publicly available documents on how these criteria are applied, and to what extent systematic methods are used to apply these criteria.

Canadian global health research initiatives increasingly rely on international cooperation and develop joint programs involving a number of funders. An example of this approach is the Grand Challenges Canada program ‘Saving Lives at Birth’, which is undertaken in cooperation with the United States Agency for International Development (USAID), the Government of Norway, the Bill & Melinda Gates Foundation and the United Kingdom’s Department for International Development. As a large global health donor, the Bill & Melinda Gates Foundation is a popular partner for Canadian global health initiatives as for many other public initiatives. The Foundation has, however, been criticized for not being sufficiently transparent and accountable in its prioritization process [20, 21]. As a private foundation, it is not required to be as accountable in how it prioritizes its work as public sector organizations are. However, with increasing amounts of public funding going to support joint initiatives with the Foundation, there is a risk that transparency and public accountability will be diminished.

Focus on research and development capacity in developing countries

Many of the Canadian global health initiatives have a strong focus on building research and development capacity in developing countries. Building such capacity is, for instance, a core function of IDRC, and the act to establish the Centre states as one of its key objectives: “to assist the developing regions to build up the research capabilities, the innovative skills and the institutions required to solve their problems” [22]. This is also reflected in GHRI documents, which report that by 2011, the initiative had provided training to approximately 10,000 people [7]. A total of 18% of this involved formal training of individuals, most often for a Masters degree. In addition, the GHRI contributed to building capacity in 266 organizations, with 73% of the organizations in low-and-middle income countries.

In general, CIHR (apart from GHRI) and Grand Challenges Canada appear to be less focused on capacity-building in developing countries as a part of their global health research and development. CIHR emphasizes supporting researchers in Canada, mostly at universities, public research organizations and hospitals, while Grand Challenges Canada emphasizes solving challenges. Solving challenges may involve capacity-building efforts, but some of its calls, such as a ‘Saving Brains’ call from July 2014, highlight that Grand Challenges Canada will not fund capacity-building initiatives alone, and its most recent Annual Report does not report metrics on capacity-building efforts.

However, the Canadian Coalition for Global Health Research does focus on capacity-building efforts, and one of its core goals is to strengthen the capacity of global health researchers, institutions and systems [23]. The coalition views strengthening capacity as an important contribution toward promoting greater equity in health around the world and organizes summer educational programs for strengthening global health research as well as other mentorship initiatives.

Other Canadian organizations also have some capacity building efforts aimed at developing countries in areas that support global health innovation. The Faculty of Law at the University of Ottawa has, for example, organized training courses in intellectual property management aimed at African countries. The Joint Centre for Bioethics at the University of Toronto has provided graduate bioethics training to health personnel in a number of developing countries in order for them to strengthen their local capacity in
handling bioethics issues related to global health development. The Sandra Rotman Centre has also provided support to projects in bioethical issues supported by the Bill & Melinda Gates Foundation. Health Canada has further offered capacity building training to drug regulators in China and in some African countries, including Malawi. The training includes a focus on management of clinical trials and could thus contribute to strengthening abilities to develop new health products.

Canada does, thus, have a clear capacity-building role in global research and development. It appears, however, to be more focused on building capacity in health systems research, rather than on product/services research and development, even though a number of smaller initiatives support various aspects of innovation training.

**Focus on supporting cooperation and networks**

Several Canadian global health initiatives have a strong focus on supporting cooperation and networks. In general, both CIHR and IDRC emphasize supporting cooperation, and have supported numerous networks. For CIHR, most of the networks involve Canadian researchers, but they have also dedicated funds to support research cooperation with the emerging economies of China and India.

One of IDRC’s core objectives cited in the IDRC Act is to “foster cooperation in research on development problems between the developed and developing regions for their mutual benefit.” 22. Their work involves supporting cooperation between Canadian researchers and researchers in developing countries, as well as supporting cooperation amongst researchers in developing countries, or South-South networks. GHRI includes, for instance, the Teasdale-Corti Global Health Research Partnership Program, which supports global health research teams, and the Africa Health Systems Initiative, Support to the African Research Partnerships program, which incorporates support for networks in Africa. These initiatives include cooperation by research users to enhance the relevance of the research, as well as cooperation that crosses national boundaries and encourages sharing expertise.

Grand Challenges Canada also aims to stimulate both these types of cooperation. For example, it encourages cooperation between global health researchers and private sector organizations, as will be discussed further below. It also has included a focus on supporting networks, such as the Mental Health Innovation Network between researchers and policy makers from the London School of Hygiene & Tropical Medicine and the World Health Organization, which focuses on mental health issues in developing countries.

In addition to supporting cooperation and networks aimed at global health problems in developing countries, Canadian initiatives incorporate a network perspective in their cooperation with other funders. Both IDRC and Grand Challenges Canada involve cooperation among Canadian funders in their very design. As mentioned above, they also cooperate extensively internationally, and have set up a number of programs supported by other governmental entities as well as foundations, such as the Bill & Melinda Gates Foundation.

**Focus on applicability and innovation**

Canada’s initiatives in global health research and development tend to be applied in focus. This applied focus is, however, not necessarily represented in product development. Within Canada’s global health research there is substantial emphasis on strengthening health systems in developing countries, so they are better equipped to deal with the health problems that confront them. There is also an applied focus in terms of shaping health policies. This health system and health policies focus, is for instance, strongly
reflected in the GHRI. An evaluation of the GHRI showed that the initiative was leading to changes in practice, such as in HIV prevention; that it was leading to changes in health systems, such as in systemic adjustments in order to offer better health services for children; and that it was leading to use of research evidence by decision-makers [7].

With respect to technology transfer for production and innovation of new health products and services, the impact of Canadian initiatives has been uneven. Canada carries out some technology transfer activities to enhance global health. A survey on Canada’s health biotechnology firms’ cooperation with low-and-middle income countries showed that the most-frequently cited reason for their cooperation with developing countries was to gain access to these countries’ markets (66% of the cooperation initiatives) [24]. However, the second most common reason that the Canadian firms cited involved technology transfer and to providing knowledge to their partners in developing countries (37% of the cooperation initiatives). Canadian health biotechnology firms are viewed as having strengths in the health biotechnology field, in demand in developing countries. It is, however, notable that cooperation was almost entirely initiated by the firms themselves, and only seven out of 82 collaboration initiatives received government support for initiating the co-operation. Cooperations are, thus, not likely to result from organized efforts by the Canadian government to transfer health technologies to developing countries.

There are also examples in which Canadian global health research has had an applied orientation and successfully identified candidates for new and improved health products, but Canadian organizations have not then developed these candidates beyond the research stage. As discussed above Canadian researchers are active in researching the Ebola virus, and researchers at the Public Health Agency of Canada’s National Microbiology Laboratory developed a vaccine candidate, VSV-EBOV, to prevent Ebola infection [25]. Animal studies in primates have been carried out and have shown the vaccine to be both effective in preventing the disease and in reducing the severity of the disease in already infected animals.

The Public Health Agency of Canada, however, licensed the technology in 2010 to a small biotechnology firm from the United States called NewLink for just over CAD $200,000. During the current Ebola outbreak, the need for an effective vaccine has surged, but NewLink’s clinical trials in people only began in the fall of 2014. There has been some discussion that the development of the vaccine has been slow since NewLink is not experienced at taking vaccines through the regulatory process and lacks production capacity [26]. This is a powerful example of how promising global health research conducted in Canada makes limited contributions because the innovation plans and innovation efforts for developing global health products are incomplete.

Grand Challenges Canada supports not only global health research but also global health innovation. The organization has presented its conception of innovation involving integration of knowledge based on science, social realities and business development [27, 28]. According to this, “scientific and/or technological innovations have a greater chance of going to scale and achieving global impacts if they are developed from the outset with appropriate social and business innovation – an approach that we call integrated innovation™” [27]. This echoes the innovation systems literature. The literature emphasizes that innovation is context-specific and incorporates both science-based and experience-based learning, with the latter incorporating social as well as business actors and context [29-32]. Without such integration, innovation is not likely to be successful.

To support innovation, Grand Challenges Canada has created a special program called ‘Transition to Scale’ that focuses on supporting innovators who want to have an impact on global health. Grand Challenges Canada’s early work in this area started in 2011, when it cooperated with the Bill & Melinda Gates Foundation to invest in point-of-care diagnostics projects in Canada and in low-and-middle income
countries. These projects had earlier received support from the Bill & Melinda Gates Foundation’s ‘Grand Challenges Explorations program’. In 2013, Grand Challenges Canada launched its ‘Transition to Scale’ program, which is based on an internal pipeline from projects the organization has previously supported. Grand Challenges Canada has developed a review process and scaling platform, and has established an investment committee of individuals experienced in raising venture capital, impact investing, and development and social innovation to provide advice on investments. According to the newest annual report, the committee has reviewed a total of 25 project proposals and allocated CAD $9.2M [10]. As this project has only been in operation for a year and a half, it is too early to evaluate the impact of these investments and their contribution to innovation.

It is, however, important to keep in mind that innovation needs a systemic approach [29-32]. In order for innovation to take place, multiple organizations need to contribute both scientific and experience-based knowledge, and there need to be active knowledge flows and alignments between organizations. In many of Canada’s global health efforts, these organizations are typically located in more than one country and innovations are embedded in diverse innovation systems. It is challenging to carry out the alignments necessary for innovation to take place, particularly when it calls for international cooperation. Research on international cooperation in health biotechnology shows that misalignments often hinder the global health innovation process [33, 34]. For instance, the regulatory systems in countries that cooperate in development of health products may not be well aligned. The information that needs to be submitted, tests and other requirements are quite different from one regulatory system to another, which puts an additional burden on globalized innovation.

There has been some discussion that Grand Challenges Canada’s focus on integrated innovation orients their global health efforts towards too much of a business focus. Research has been carried out on the experiences of four new investigators who had received a grant under the ‘Rising Stars in Global Health program’ [35]. The investigators spanned several different disciplines, and the researchers were interviewed about their experiences and views of the ‘Rising Stars’ program. A recurring theme in the analysis was that, while integrated innovation has a strong potential for global health, an overemphasis on commercialization and corporatization may have detrimental effects: “...a business focus seriously limits the potential for global health innovations to reach the most marginalized populations in low-and-middle income countries, who may not present a viable market.” [35]. The authors do not argue that commercialization should be ignored, but recommend that Grand Challenges Canada build a strong commercialization-support program in which grant recipients are connected with potential funders. These funders could be of various types: non-governmental organizations, drug companies, foundations or private investors. The authors also emphasize that Grand Challenges Canada should value social returns on investment as equivalent to financial returns on investment. This is the case particularly when the work is focused on health products aimed at marginalized populations in low-income countries. The authors argue, in fact, that a stronger focus on social return of investment may be a key to promoting global health equity.

The research presented here is, however, based on a small sample; perceptions of four Grand Challenges Canada recipients. Clearly, further, research is needed to confirm these views and establish whether these concerns are more widespread. There is also a lack of external evaluation of the GHRI initiative as well as of other Canada’s global health initiatives and there is a demand to confirm their impacts by impartial observers.

**Conclusion**

As this discussion has shown, there are a number of initiatives in Canada aimed at strengthening global health research and innovation. Significant contributions have been made in several areas, including
research on the Ebola virus; research on maternal and child health; and on of health systems operation. In recent years, there has been considerable focus and prioritization of maternal and child health, and time will tell what the impacts of this focused approach will be. Canada has also initiated a number of projects to promote global health capacity-building and cooperation in different fields across the world. An in-depth evaluation of these initiatives is needed and would cast light on the strengths and weaknesses of these efforts and identify strategies to strengthen them and their contributions to global health.

The discussion above has also delineated the differences between the key Canadian funders of global health research and development. CIHR is mostly concerned with supporting fundamental health research, mostly carried out by Canadian universities, hospitals, or public research organizations. IDRC and GHRI support mostly research on health systems and health policy while Grand Challenges Canada supports innovation focused efforts. Together they support a wide spectrum of activities.

The limited observations on Canada’s contribution to global health innovation suggests that Canadian efforts in this field may need to be better integrated into the overall Canadian innovation system and/or in the innovation systems of the focal developing countries. In order to have more impacts and contribute more to global health innovation, there is a need for a more comprehensive approach to innovation planning, as well as a systemic perspective. Successful innovation will require input from several organizations and knowledge flows and alignments among them. To contribute to a larger extent to global health innovation, Canada needs to understand better the key challenges of its efforts to promote global health innovation, and identify evidence-based strategies to address these challenges. With more coherent and concerted efforts, Canada’s global health initiatives can be strengthened and have greater impact around the world.
References

Assessment/Next steps on WHA61.21- Global Strategy and Plan of action on Public Health, Innovation and Intellectual Property
PCBR, THSTI: ANALYSIS OF WHA 61.21 ELEMENTS: INDIA COUNTRY PROFILE

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Executive Summary

The analysis shows that India has come a long way making rapid strides to bring universal health to all its citizens and the country have formulated major programs to reduce both communicable and non-communicable diseases. India is promoting both modern and traditional medicine as well as promotion of healthy living which will be bringing holistic health systems to all Indian citizens. After the economic liberalization, India has embarked upon path of development. As more economic growth is achieved in the country India will concomitantly find more investments for R&D. Health innovations produced in India will be more affordable, accessible in India and the region, will be reaching the masses in lesser time. In the meantime the government has also brought about legislation to build more administrative structures to regulate basic, translational and clinical research in the country. In addition new ethical guidelines are in place for both animal and human experimentation. Good manufacturing practices are now a norm as local industry has to complete globally in an open liberalized economic scenario. The Indian government and private sector have invested in R & D in the last decade and will be continuing to do so in building up of new health research infrastructure and medical colleges respectively in the country. Profiting from the young population, gradually a large pool of manpower is being trained in the health sector. Being the largest country in the SEARO region with largest infrastructure and trained manpower, India is in a strong position to help other countries in SEAR in achieving their health programs especially smaller countries like Bhutan, Maldives and Timor Leste. Reciprocally India also learning from the successful public health from other countries and helping in adopting propagating them across the region. The major contributions that India can make are as follows;

(1) Human Resource Development for Health Research
(2) Grants in Aid scheme for inter-sectoral convergence & promotion and guidance on research governance issues
(3) Infrastructure Development for Health Research (Establishment of Multi-Disciplinary Research Units in Government Medical Colleges).
(4) Establishment of Model Rural Health Research Units in States
(5) Establishment of a network of Laboratories for Managing Epidemics and Natural Calamities

We have challenges in SEAR but we can be overcome them. Region can achieve health for all by innovations through concerted efforts by promoting health R & D capacity.

a) Strengthening R & D initiatives to address local priorities by ensuring inter-country collaboration and adequate and sustained funding especially in smaller countries in the region to help in appropriate policy making and program management
b) Strengthening multi-sectoral research through collaborative approach to achieve UHC and MDG goals
c) Significantly Improving the quality, standards and access to health systems
d) Mobilizing programmatic and policy support to improve program management and supplementary health research
e) Implementing and evaluating innovations, technology and interventions contributing in universal health care ensuring availability of mechanisms for their standardization and accreditation
f) Providing strong support for developing uniform mechanisms for monitoring and evaluation
Preface

India adopted a policy of manufacturing affordable generic drugs with the 1970’s patent regime under which pharmaceutical products could not be protected through patents, but only the processes for producing them. The pharma sector with Indian scientific acumen produced new ‘processes’ for cost effective chemicals that was source for making copies of many drugs available at higher prices elsewhere in the world. After 2005, India as a signatory to TRIPS agreement, had to adopt a ‘product patent’ regime hence it was no longer possible to produce copies of products even if the processes were new. It is now almost a decade after implementation of new patent regime and there is a need for an analysis and assessment to gauge how health systems and access to health care interventions have been impacted by the TRIPS regime.

In the light of the TRIPS agreement, and assessing its effect on developing economies, the WHA 62.16 resolution dated 22 May 2009 on Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property proposed “to conduct an overall programme review of the global strategy and plan of action in 2014 on its achievement, remaining challenges and recommendations on the way forward and report to the Assembly in 2015 through the Executive Board.” The earlier WHA resolution 61.21 identified a number of deliverables under Global Strategy and Plan of Action on public health, innovation and intellectual property (GSPA) and aims to promote new thinking on innovation, transfer of technology and access to medicines. In this context, the mapping of health and R & D status in India is important.

The analysis carried out by .... shows India has the largest scientific pool of human resources in the region and there is rapid increase in quality and numbers of science professionals. With more financial and training incentives, as well new infrastructure and research capacity being built, the nation can become a hub for health innovations and manufacturing in all sectors. There are several health and related sectors which need improvement through strong policy recommendations. The need for more investment in research and development in the field of health with adequate training and retaining of human resources with the country is important for better health. In addition widespread availability and affordable health technologies are required.

The analysis of WHA61.21 has been taken up logically through each of the eight elements as follows:
Element 1: Prioritizing Research and Development Needs

India has created new, innovative technologies in the last decade or so by strengthening its commitment and investment in the health research and development (R & D). This has led India to become the hub for low cost yet high quality generic medications internally and for the global procurement. The benefits of investments made in R & D in the earlier years have made India a Center of excellence in health R & D. However, the investment needs to be escalated and retained to maintain the progress.

Need for Prioritization of Health Research and Development

Research priorities have been identified and set by some international organisations like WHO SEARO which have set its goal to assist Member States to reverse the trend of communicable diseases, by reducing morbidity and mortality, improving the quality of life, which will support towards achieving the Millennium Development Goals (MDG) as well as poverty reduction in the coming decade.

The WHO-India Country Cooperation Strategy (CCS) 2012-2017, has been developed with the Ministry of Health and Family Welfare, Government of India to help to improve health and equity in India. Hence, WHO- CCS through consultations with Ministry of Health has identified priority areas as: Combined morbidity in both Communicable and non-communicable diseases, health of mother and child, international health regulations, pharmaceuticals, quality of research, stewardship, and transitional services.

National Institutes of Health across the globe supports many concepts and tools central to understanding and improving health but also conducts the clinical and translational research that transforms discoveries into medical practice. It has set up research programs as per the priority areas like: AIDS, Behavioural and Social Research, Diseases prevention, Portfolio analysis, Chronic diseases, Infectious diseases, Personalized medicines and new technologies, Health at all ages, Research infrastructure program, Research on women’s health, Stem cells etc.

Research priorities set by some of the national bodies are Vision of National Health Research Policy (2011) which aims to

- identify priorities for effective and ethical health research in accordance with national health agendas and global commitments,
- foster inter-sectorial coordination to promote innovation leading to effective translation to indigenous production of diagnostics, vaccines, therapeutics, and medical devices etc, focus on the vulnerable, the disadvantaged and the marginalized sections of society, strengthen national networks,
- set strategies and mechanisms to assess the cost effectiveness and cost benefits of health interventions and create, nurture human resources and infrastructure, encourage international collaborative research contributes to national health.

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61 World Health Organization. Advisory committee on health research Report To The Director-General on its fifty-first session Held at WHO Headquarters, Geneva; 16-18 March, 2009 (WHO/ACHR 51/24)

http://apps.searo.who.int/PDS_DOCS/B4414.pdf

Department of Health Research (DHR) helps in promotion and co-ordination of basic, applied and clinical research, clinical trials and operational research. It caters to the areas of health, medical, biomedical, education, and medical profession by developing of infrastructure, manpower and skills and managing related information also. It facilitates the Inter-sectoral coordination and promotion of public-private partnership, coordination between organisations and institutes under the Central and State Governments, International cooperation in medical and health research.

DHR also helps in strengthening Indian Council of Medical Research (ICMR) as fulcrum of this Department in generating scientific knowledge for translation and implementation and give impetus to research and innovation. Some of the flagship programmes of ICMR are Vector Borne Disease Science Forum, Translational Research, Department of Science and Technology, The Technology Development Board, R & D priorities of Council for Scientific and Industrial Research, Traditional Knowledge Digital Library /TKDL

Defence Research and Development Organization (DRDO) grants funding for Life Sciences in Institute of Nuclear medicine and Allied Sciences (INMAS), other universities and institutes, Ministry of Human Resource Development- http://mhrd.gov.in/: It supports all the Indian Institutes of Technology IITs, newly formed Indian Institute of Science & Research (IISERs), etc. for open ended R&D.

Ministry of Chemicals and Fertilizers- http://pharmaceuticals.gov.in/: National Institute of Pharmaceutical Research (NIPER), Bengal Chemicals & Pharmaceuticals Ltd, and Hindustan Antibiotics Ltd. are supported through Venture Capital Fund by the Ministry,

Department of Atomic Energy (DAE) - http://dae.nic.in/: It supports training facilities and funding research in the universities and national laboratories (TATA Memorial Centre (TMC), Advanced Centre for Treatment, Research and Education in Cancer (ACTREC) through the Board of Research in Nuclear Sciences (BRNS).

Ministry of Earth Sciences - http://www.dod.nic.in/: Provides grants to Department of Ocean Development, Universities and Institutes to carry out research on “drugs from Ocean” in collaboration with CSIR.

University Grants Commission (UGC)-http://www.ugc.ac.in/ and State Governments: Few of them have started biotech development funds of their own to invest in local companies. Andhra Pradesh Industrial Development Corporation, Karnataka State Industrial Infrastructure Development Corporation, Kerala Venture Capital Fund are few examples.

Different funding schemes to sustain the R & D of Health sector
Apart from the above mentioned major programs, there are public, private, NGO and international funding agencies to support R &D.

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64, Annual report of Department of Health Research, National Health Research Policy. 2011-12, 21-26
Public Funding sources are: Department of Science and Technology, Department of Scientific & Industrial Research which allocates financial support for science development, gives National Awards for outstanding in-house R&D achievements of industry, Department of Biotechnology.

Private Funding sources are: Pharmaceutical companies have partnered with public organizations, NGOs to develop safe, cheap and quality therapeutics, diagnostics etc. Dr Reddy’s Group with University of Hyderabad has formed Institute of Life sciences. The Chatterjee Group of Companies and CSIR has partnered to create Institute of Molecular Medicine, New Delhi. Several Bio Pharmaceutical Companies have started Contract Manufacturing.

Non-Governmental Organizations such as:
- a) The Sir Dorabji Tata Trust has supported many leading institutions with endowment grants.
- b) Child Health Foundation, USA has funded Sahara in Orissa; and Medical Society, Andhra Pradesh for prevention and treatment of HIV-infection; Jeevan Rekha Parishad, to give away ORS to refugee camps in Orissa.
- c) Society for Applied Studies, a non-profit organization in Kolkata and New Delhi conducts clinical trials, in collaboration with several Indian and foreign public and private agencies.

International Funding: Many international organizations/ institutional arrangements are actively involved in scientific activities in India; some of them include:

- a) World Health Organization (WHO), Geneva
- b) Foundation for Innovative New Diagnostics (FIND),WHO
- c) Tuberculosis Diagnostics Initiative (TBDI),WHO
- d) WHO-the global stop TB partnership’s working group
- e) WHO- Special Program for Research and Training and Tropical Diseases (TDR)
- f) UNITAID
- g) The Global Laboratory Initiative of WHO Stop TB
- h) The Global alliance for TB drug development (TB Alliance),
- i) Medicines for Malaria Venture
- j) Drugs for Neglected Diseases Initiative (DNDi)
- k) Program for Appropriate Technology in Health (PATH)
- l) Danish International Development Agency(DANIDA)
- m) Department for International Development (DFID)
- n) Global Fund to fight against AIDS , TB and Malaria/ (GFATM)
- o) Institute for One World Health,
- p) International vaccine Institute,
- q) Foundation Merieux, France
- r) Bill & Melinda Gates Foundation, USA
- s) The Howard Hughes Medical Institute, USA
- t) The National Institutes of Health, USA
- u) several UN organizations (UNESCO UNHCR; UNICEF, UNFPA, UNDP, UNODC)
- v) the World Bank etc.

An example of International funding for Promoting R & D is Drugs for Neglected Diseases Initiative (DNDi) work in India. Several drugs in India like Ambisome, Miltefosine and Paramomysin are registered and used for the treatment of Visceral Leishmaniasis. The Phase III trial conducted by DNDi and its partners in 2010 in India demonstrated the efficacy of combination therapies based on AmBisome®, miltefosine and paromomycin. Another new drug, Scyx 7158 as a treatment for VL screening is ongoing. Also, there are several producers in India in the process of developing generics of AmBisome®.

For HIV, Cipla has been partnered with DNDi for the Two 4-in-1 LPV/r based fixed-dose Combinations study. ASAQ Winthrop, for malaria through ICMR and ASMQ FCD trials is ongoing.
Formulating explicit prioritized strategies for research and development
It has been noted that a different set of challenges to health has joined the familiar problems of infection and malnutrition in developing countries including in India. Over the next 25 years, most developing countries are likely to be exposed to non-communicable diseases and these diseases become their leading causes of disability and premature death. Hence, there is a need for India to engage and prioritize more concerted effort towards R &D in these areas. Simultaneously, emerging and remerging diseases as well as neglected diseases should remain a focus of attention.

Role of Biotechnology in prioritizing Health R & D
The cooperation within health science biotechnology with scientists, clinicians, commercial partners, collaboration with other countries have enabled a congenial atmosphere in the R & D area for biotech product and process development. The Centers of Excellence and Program Support in areas of Biotechnology and Information and Communication Technology (ICT) R&D has also made remarkable progress.

Several success stories are being reflected in the recent past with reference to the polio eradication, introduction of 4 new vaccines, India as leading producer of low cost, drugs, and vaccines. Indian manufacturers produce 80 percent of the drugs used in donor-supported AIDS treatment programs and are major suppliers of malaria drugs as well. Indian Companies sell rapid tests for HIV and malaria to programs in Africa and other places across the globe, while Serum Institute of India alone supplies vaccines used in 140 countries.

Role of Clinical Trials in the Health R & D
Indian clinical trial registry has been established to enrol all of the trials carried out in the country details are at: (http://ctri.nic.in/Clinicaltrials/login.php)

Encouraging research and development in Traditional Medicine
The 11th Plan as well as by DBT are engaged in this area of R&D in traditional medicine. Numerous nutraceutical combinations have entered the international market through exploration of ethno pharmacological claims made by different traditional practices. AYUSH,ISM and Ayurvedic system of medicine has shown promising role in translational medicine in order to overcome malnutrition and related disorders.

India practices medical traditions like Ayurveda and siddha still practiced in some parts of India. However, the integration of such systems into modern medicine practice faces challenges.65 AYUSH brings a new impetus with substantial budgetary support. India is also setting up an All India Institute of Ayurveda on the lines of the six All India Institute of Medical Sciences set up in cities across the country. The institute will have AYUSH departments, with special focus on Ayurveda

medicine. Currently, AYUSH practices lack hard evidence and need large-scale, double-blind, randomized, multicentric clinical trials which can be published in peer-reviewed international journals to validate the claims of Ayurveda or such systems. Practitioners of Ayurveda need to follow the experimental methodology of modern science which strengthens the mixing of the practice of Ayurveda with modern medicine at AIIMS.

China has a culture of pushing for traditional Chinese medicine through significant modernization of traditional Chinese medicine and integrated it into its health-care system, whereas, India has recently begun to provide significant impetus to traditional medicine. India needs a proven and documented track record is essentially needed to promote the systems to reach international acceptance as scientific disciplines.66

**Element 2 Promoting Research and Development**

**Need for promotion of Health Research and Development (R & D)**

R&D investment facilitates new products and services which drive growth, and create new jobs. R&D spending remains concentrated in the developed countries; however, it has increased distinctly in some of the emerging market economies namely in India and China. India has initiated several efforts for the development of health and biotech products by both private and public organizations. The Industrial Biotech pipeline initiatives for the Therapeutic Products in the areas of Type I, II & III Diseases have promising future.

**Mapping global research and development**

As a part of this activity, the mapping focussing research capacity on tropical diseases was conducted in 2011 under a WHO-SEARO project in 7 regional countries, among which India carried out detailed exercise and brought out a report67. The work opened the scope for promoting centres of excellence and establish network with other institutions. This can help to bridge the gap for qualitative research and other allied activities of R & D. In 2011, the reports were presented in the Regional meeting in India.68

The need to establish Mapping of health R&D among the ASEAN-member countries was felt to be an integral part for the landscaping of the ASEAN Network for Drugs, Diagnostics, Vaccines, and Traditional Medicines Innovation (ASEAN-NDI). The exercise was conducted from November 2009 to December 2010, further strengthened by the review of Elsevier’s Scopus database. The exercise

66 Indian System of Medicine - Industry Report. ID: 349608; July 2006; Region: India; 156 Pages ; Cygnus Research.

67 [http://apps.searo.who.int/pds_docs/B4922.pdf](http://apps.searo.who.int/pds_docs/B4922.pdf)

68 Ganguly, N.K. Final Report on WHO Project Mapping of National Centres/Institutions on Tropical Diseases in India
helped to assess the product R&D landscape on infectious tropical diseases, non-infectious diseases and other preventable diseases caused by injuries.

**Gaps Identified in the area of Health R & D**

The National Pharmaceutical Pricing Authority’s (NPPA) decision to impose ceiling prices on 348 essential drugs under the National List of Essential Medicines (NLEM), by adopting a simple average price formula, has been to the industry’s disadvantage and will deter investments in research and high quality manufacturing and distribution; Investment in R & D has increased but there is decline in approval of new drugs; Top-selling medicines are going out of patent but are not replaced by new patented products; Greater focus on emerging markets which offer opportunities for rapid growth; India needs orphan drug developers and Orphan Drug Act is not yet developed to attract the Indian pharma companies. Many regulatory and commercial incentives need to be provided under this Act; Declined support in traditional medicine R & D; Progress in product development for type II and III diseases is very uneven; To acquire an overview of methods for research priority setting used by various departments; To identify a potential need for normative work on the process of research priority setting; To emphasize more on Product Development Partnership (PDP) at National level and More effective public–private partnership.

**Element 3: Building and Improving Innovative Capacity**

Success in Biomedical innovation requires scientists, engineers, and managers with the right mix of skills, publicly supported research with strong links to industry, supportive regulatory system, functioning infrastructure, demand and supply of health services, financing for product development and, of course, markets for products. India is making purposeful efforts to build their scientific and technological capacities.

Scientific and technological capacity to meet R & D needs at least three core components-

**1. Developing skilled labor:**

The government needs to make scientific research a more attractive career option for younger generation. Institutions whether local communities or national R&D centres are the ones that mobilize and use the skills/expertise as well as design and implement policies. Institutions consist of: Public research system (68%), Higher educational institutions (14%), Private business enterprises and transnational corporations (30%), Public policies on science and technology and Non-governmental research institutions aided by both public and private sources.

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69 Biocon chief seeks PM’s intervention to solve issues being faced by Pharma industry. Monday, July 28, 2014.
70 https://www.oecd.org/sti/Venni%20V.%20Krishna%20%20Centre%20of%20excellence%20as%20a%20tool%20for%20capacity%20building%20-%20Case%20Study%20India.pdf
2. Funding for Capacity building:

Public Sector: Many research institutes fall under the purview of DBT, DSIR, and ICMR, and much of the public-funded research that takes place in India occurs within these. The World Bank Group was catalytic in seeding the VC industry in India; in fact, the International Finance Corporation (IFC) remains one of the most significant PE investors in the country. In 2010, the IFC made $223.4 million worth of PE investments in India across 14 deals, which is about $62 million more than the next top PE investor. When investors do fund life science firms, they usually support mature projects rather than early high-risk work. Although social impact investing, or investing in businesses or organizations that pursue both financial and social returns, is also gaining currency in India, so far, social businesses in India tend to follow a health service–based business model or market technologies that require considerably less R&D than drugs or vaccines. Recognizing that overall investment in the life sciences has been low, the government of Andhra Pradesh partnered with Dynam Ventureast to launch a $37 million venture fund dedicated to biotechnology investments. After the fund’s establishment, the World Bank Group’s IFC contributed $4 million in equity to it. The fund’s activities are not limited to health—in 2004, it provided about $17.7 million to biotech firms.

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73 Naru, S. Presentation. The biotech investment opportunity in India. Presentation at ADIPC Venture Capital Limited


75 4Grant Thonton (2011)


Non-governmental organizations: DFID supports long-term programmes to help tackle the underlying causes of poverty. In 2008/09, the department provided £5.5 billion of aid to poorer countries. DFID’s development capital investments will help a chain of affordable hospitals serve 1.2 million rural patients in low income Indian states by 2020\(^79\).

Recently, the Indian government has launched a range of initiatives to address weaknesses in the biomedical innovation system, like developing bio-clusters, schemes for public private partnership, to provide incentives to firms or companies to conduct drug research and development\(^80,81\). The other programs are Science, Technology and Innovation Policy 2013 Programme on Innovation, Higher education and research for development (IHERD) to build centers of excellence (CoE) by developing inter-university centers for education/ research and inter-institutional centers (IICs). National Biotechnology Development Strategy (2007-current) allocated more funding to programs supporting public-private partnerships. The most prominent programs to support health R&D within firms are the Biotechnology Industry Partnership Programme, the New Millennium Indian Technology Leadership Initiative, the Small Business Innovation Research Initiative, Technology Development Board (TDB), Biotechnology parks and clusters, Grand Challenges Program for Vaccines.

Policies undertaken to promote traditional medicine are: setting up of more National level Research Institutes in the field of Traditional Medicine (from 58 in 20002 to 73 in 2012); establishment of a new Traditional and Complimentary division or delegation of govt. staff to Traditional medicines issues; India and Indonesia contribute to the International Regulatory Cooperation for Herbal Medicines (IRCH); a website HerbalNet was launched by WHO as a “Digital Repository” and “Delhi Declaration” signed by the health ministers of the member states of WHO SEARO region to cooperate, collaborate and provide mutual support to each other in all fields of traditional medicine. India has 686310 registered AYUSH doctors, 3204 AYUSH hospitals, 61583 beds(5 beds per 1,00,000 population)\(^82,83\)

Initiatives taken to improve innovation in health products include the 2005 Patent Amendments Act which does not grant new patents for new uses of a known substance or for modifications to a drug unless the changes make the drug significantly more efficacious. This allows Indian companies to market generic drugs in India more quickly. Other positive interventions are: 100% FDI in the

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\(^82\) Vijayraghavan & Dutz (2012). Department of Science and Technology. Drugs and pharmaceutical research. (www.dst.gov.in/scientific-programme/td-drugs.htm#1, accessed on 18 Nov, 2014)

healthcare sector; reduced and rationalized the customs duty on medical technology imports in the Union Budget and removal of trade barriers to encourage trade in medical technologies.

Regulatory Environment in India presents a complicated landscape for health technologies, especially those involving biotechnology and genetically manipulated organisms. At least three ministries, as well as a number of small departments or agencies, have some role in regulating biomedical R&D.\textsuperscript{84,85}

Few examples of need based investment in research which has been implemented in different parts of the world, for high burden diseases such as Tuberculosis, Diabetes and Cardiovascular diseases are New diagnostics for tuberculosis: a validity assessment of the Xpert® MTB/RIF assay in Azerbaijan, India, Peru and South Africa; the “polypill” to reduce deaths from cardiovascular disease: a randomized controlled trial in India and Self-expanding diabetes clinic.

**Element 4: Transfer of Technology**

Technology transfer by ICMR\textsuperscript{86} can be broadly divided into the area of Communicable Diseases and of Non-communicable Diseases. For Communicable Diseases, 43 technologies that have been generated for commercialization; while in the area of Non-communicable Diseases, 19 technologies have been generated for commercialization. (another way to divide it is drugs (10), diagnostics (24), Vaccines (6), Medical devices (5), and Vector control technologies (13)). Those technologies that do not fall within any of the aforesaid categories albeit few (4), may be classified as “Others.\textsuperscript{87}"

Besides the technologies that have already been transferred by ICMR, two technologies are available that are ready for transfer. These are (i) Loop mediated isothermal amplification (LAMP) assay for a reliable and rapid diagnosis of Leishmania infection; and (ii) Immunodiagnostic reagent for the detection of P. vivax antigen.\textsuperscript{88}

The information on technology transfer by DBT\textsuperscript{89} has been based on data collected from the Annual Reports (2008-09 to 2012-13). CSIR’s research endeavors have led to the development of process technologies for generic drugs in 17 disease areas. For example the conjugate Hib vaccine first licensed in 1987, but until 1998 was not widely used in developing countries. The vaccine was

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\textsuperscript{84} Indian Private Equity and Venture Capital Association. (2007). Venture capital and private equity in India. Presentation
\textsuperscript{87} Annual Report of Controller General of Patents, Designs & Trade Marks; (Web site: www.ipindia.nic.in, Accessed on 5 Jan 2015)
\textsuperscript{88} http://icmr.nic.in/icmrnews/IPR_tech/ipr_lamp2.htm
\textsuperscript{89} DBT Annual Reports, Govt. of India (2008-09; 2009-10; 2010-11; 2011-12; and 2012-13) (http://www.dbtindia.nic.in/outreach/annual-report, accessed on 25 Nov 2014)
expensive compared with other EPI vaccines; there were no developing country manufacturers; and in many regions the disease burden was not known, and so there was little justification for introducing a vaccine. Between 1998 and 2001 several Hib technology transfer activities were undertaken, including from the Netherlands Vaccine Institute (NVI) (the Netherlands) to three manufacturers in India, and in 1998 from GlaxoSmithKline (GSK; Belgium) to one manufacturer in Brazil, which immediately implemented the vaccine in the national immunization programme, resulting in an immediate reduction in disease incidence. As a result of these technology transfer activities, there was an increase in vaccine capacity and a marked decrease in price. There are now eight prequalified (UN agency) manufacturers providing Hib-containing vaccines. This increased capacity, supplemented by epidemiological studies by WHO to demonstrate that the disease was prevalent in many countries, and with financial assistance from GAVI to enable the poorest countries to purchase the vaccine, has enabled the vaccine to be introduced into many national immunization programmes.

Another example would be Hepatitis B vaccine Recombinant introduced in industrialized countries by GSK and Merck in 1983. For over a decade the cost was in the region of US$ 100 per dose, and there was no significant use of the vaccine by developing countries. In the late 1990s technology transfer to the Republic of Korea, India and Brazil resulted in a price drop initially to US$ 5–7 per dose. This increase in supply, the entry of purchasing agencies and financial assistance from GAVI drove demand up and price down to less than US$ 0.3 per dose. As a result the vaccine is now in most national immunization programmes, and hepatitis B vaccine coverage is increasing continually. Distribution of technology recipients by country, demonstrates that although 13 countries have received vaccine technology transfer, the vast majority of these transfers have been to China, India, Brazil and Indonesia\textsuperscript{90}.

After analysing the technology transfer landscape, taking ICMR, DBT and CSIR as examples, it is evident that a number of technologies have been developed by these organizations. However, there is still room for improvement, More emphasis needs to be given to the translational research in order to deliver more products to the market. One of DBT’s new institutes, namely, the Translational Health Science and Technology Institute (THSTI) is geared specifically for this purpose.

**Element 5: Intellectual Property**

An analysis of the trends in patents in India reveals that the number of patents filed is similar for the years 2010-11, 2011-12, and 2012-13, while it is slightly lower for the years 2008-09 and 2009-10 \textsuperscript{91}. In general, there has been a decreasing trend in the number of patents being granted, which may

\textsuperscript{90} Increasing Access to Vaccines through Technology Transfer and Local Production, WHO 2011

\textsuperscript{91}Annual Report of Controller General of Patents, Designs & Trade Marks; (Web site: \url{www.ipindia.nic.in}, Accessed on 5 Jan 2015)
be expected as the level of stringency with which the patents are examined have increased over the years.

When it comes to filing patents, CSIR, tops the list, with just over 200 patents in 2012-13. In second position is DRDO with 73 patents in 2012-13. Importantly, it is to be noted that aside from CSIR, all the other funding agencies lag far behind with respect to the number of patents filed.\textsuperscript{92}

When it comes to patent applications and top Indian institutes and universities, the IITs top the list with just over 200 patent applications in 2012-13; followed by Amity University with 140 patents in the same year. The 3\textsuperscript{rd} and 4\textsuperscript{th} positions are occupied by the IISc and NIPER respectively (Table 3)\textsuperscript{1}. It should be noted that the comparatively higher number of patents for the IITs is because all the IIT clusters have been pooled together\textsuperscript{93}.

The National Institute of Immunology (NII) tops the list with 28 filed patents in the last 5 years, followed closely by the International Centre for Genetic Engineering and Biotechnology (ICGEB), while the Translational and Health Science & Technology Institute (THSTI), the newest institute to be established by DBT has 1 filed patent (in 2011-12) to its credit\textsuperscript{94}.

CSIR may be considered as a trend-setter and a pioneer in this area. The major institutes that have contributed to this remarkable achievement in the Health and Biotech sector include the Centre for Cellular and Molecular Biology (CCMB), Hyderabad, Central Drug Research Institute (CDRI), Lucknow, Central Food Technological Research Institute (CFTRI), Mysore, Central Institute for Medicinal and Aromatic Plants (CIMAP), Lucknow, Institute of Genomics and Integrative Biology (IGIB), New Delhi, Indian Institute of Chemical Biology (IICB), Kolkata, Indian Institute of Chemical Technology (IICT, Hyderabad), Indian Institute of Integrative Medicine (IIIM), Jammu, Indian Institute of Toxicology Research (IITR), Lucknow, National Botanical Research Institute (NBRI), Lucknow, National Chemical Laboratory (NCL), Pune and the New Millennium Indian Technology Leadership Initiative (NMITLI), CSIR HQ, New Delhi\textsuperscript{95}.

On the pharmaceutical front, a number of patents have been granted during the period 2010-11 to 2013-14. The highest number of patents has been granted to Eli Lilly and Company (34). In second position is Pfizer with 33 patents. Joint third position is held by Astra Zeneca and Sanofi with 23

\textsuperscript{92}Annual Report of Controller General of Patents, Designs & Trade Marks; (Web site: www.ipindia.nic.in, Accessed on 29 January 2015)
patents each. Two Indian companies have also made this list. These include Cadila and Panacea Biotec, with 10 and 7 patents to their credit\(^\text{96}\).

**Element 6: Prioritizing Health Care Access**

Despite progress in improving access to healthcare, inequalities by socioeconomic status, geography and gender continue to persist.

**Progress in MDGs:** Maternal mortality rate has decreased by ~50%, and was reported at 200 deaths per 100,00 live births in the year 2010 as compared to 390 a decade ago. A few states such as Tamil Nadu, Maharashtra, and Kerala have already achieved the Millennium Development Goal (MDG) of a maternal mortality ratio less than 109 maternal deaths per 100,000 live births, with multiple other states close to achieving this target. Infant mortality rate has decreased by greater than 25% over the period 2000–2009, and was reported at 50 deaths per 1,000 live births. Correspondingly, the under-5 child mortality rate (USMR) has decreased by similar percentage levels, and was reported at 64 deaths per 1,000 live births. While USMR for urban India has achieved the MDG target of 42, the rate for rural of 71 is significantly lagging the target level. Immunization coverage has increased significantly, for example diphtheria-tetanus-pertussis immunization among 1 year olds has increased from 60% to 70%, and the Hepatitis B coverage has increased from 68% in 2005 to 91% in 2010. National programs have successfully improved detection and cure rates for tuberculosis and leprosy\(^\text{97}\).

Notwithstanding the sector’s rapid growth and potential, in many respects, India’s healthcare sector falls well below international benchmarks for physical infrastructure and manpower, and even falls below the standards existing in comparable developing countries. Added to this is the mal-distribution between rural and urban areas and shortages of specialized personnel. The current ratio of beds per thousand persons is a mere 1.03 (well below the WHO norms) compared to an average ratio of 4.3 for developing countries like China, Korea, and Thailand, and in the best of circumstances is projected to reach 1.85 per thousand persons by 2012. It is estimated that over a million beds have to be added to attain this 1.85 ratio, which translates into a total investment of $78 billion (Rs. 350,830 crores) in health infrastructure. An additional 800,000 physicians are required over the next 10 years, which in turn translates into huge investments in training facilities and equipment. In order to reach even 50-75 percent of the present levels of other developing countries, the sector will require an estimated investment of $20-30 billion.


Public sector ownership is divided between Central & State governments, municipals and Panchayats (local governments). The facilities include teaching hospitals, secondary level hospitals, first-level referral hospitals (community health centres/rural hospitals), dispensaries; primary health centres, sub-centres, and health posts. Also included are public facilities for selected occupational groups like organised work force (Employees State Insurance Scheme), defence, government employees (Central Government Health Scheme – CGHS), railways, post and telegraph and mines among others. The Government of India total healthcare expenditure was 4% of GDP in 2010 and it is expected to increase to 5.5% of GDP by 2022. It has spent significantly on both awareness and delivery of healthcare through its key national level programs including National Rural Health Mission (NRHM), National Urban Health Mission, Rashtriya Swasthya Bima Yojana (Hospital Insurance Scheme) and Pradhan Mantri Swasthya Suraksha Yojana (PMSSY). The programs address issues, such as the disproportionate investment in urban cities, general lack of healthcare resources and infrastructure in comparison to international standards, lack of quality treatment, and affordability.

Successful health-sector reform in developing countries are built on sustainable service delivery models that meet reform goals while addressing community needs. When government efforts fall short, innovative private-sector solutions can offer more-efficient alternatives that provide care to impoverished populations.

Many Initiatives have been taken up to Improve Health care access such as encouraging increased investment in health. Some Successful example of approaches to overcome barriers to delivering care in low resource settings are Aravind Eye Care, Madurai, the world’s largest provider of cataract surgery, Today, Aravind treats more than 60 per cent of its patients for free, even as it remains a profitable venture. Life Spring Hospitals is a network of maternity and child-care hospitals that provides high-quality, low cost maternal services to low-income women with clear and transparent pricing. L V Prasad Eye Institute (LVPEI) touches all levels of society from primary eye care to advanced tertiary level; Health Initiatives under SEWA (Self Employed Women’s Association) modela community based, women-led primary health care programme, focusing on primary health care in maternal & child health, mental health and nutrition and Narayana Health care (NH) aims to offer quality medical care to all, called “Affordable Quality Healthcare for the Masses Worldwide” exemplifies how to make health care accessible to all

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Hence it is possible to fulfil a great social need without compromising on the profitability, which will be doable in the future if the number of interventions continue to increase such as Corporate Social Responsibility (CSR) (some good examples will be CSR activities of Biocon and Piramal Enterprise); Medical Tourism, India’s medical tourism sector is expected to experience an annual growth rate of 30%, making it a $2 billion industry by 2015. With specialty and super specialty hospitals equipped with the latest equipment and the best surgical procedures at relatively inexpensive charges there is huge potential to expand in area of medical tourism.

**Investment in financing Health Products**

**Public Health Financing:** Indian health sector, like many low and middle income countries, faces the challenge of low level public spending Some recent initiatives to augment public spending on health care include National Rural Health Mission (NRHM); National Urban Health Mission; Public Health programmes like Vector Borne Disease Control, Reproductive and Child Health Programme (RCH), TB Control Programme, Blindness Control Programme, Leprosy Eradication Programme, Iodine Deficiency Disorders Control Programme, National AIDS Control Programme and National Mental Health Programme.

**Community Programs:** The major initiative from the central government came with the launch of Rashtriya Swasthya Bima Yojana in 2008, which provided access. The Central and State government has started several schemes for health insurance such as RashtriyaSwasthyaBimaYojana(RSBY), SamajikMukt’ card, The Employees’ State Insurance Scheme(ESIS) and Central Government Health Scheme(CGHS)106. Some good examples of CHI schemes operating in the rural areas and providing protection against catastrophic health expenditure are Rajiv Aarogyashri (in Andhra Pradesh); Arogya Raksha Yojana, Yeshasvini Cooperative Farmers Healthcare System and Karuna Trust (in Karnataka); Jeevandai AarogyaYojana (in Maharashtra) and SEWA (in Gujarat). Other Community based schemes include provision of free drugs, diagnostics like Rajasthan free Medicine Scheme.

**Private Healthcare Financing includes** Debt financing; Foreign direct investment, FDI policy permits 100% foreign investments under automatic route. Drugs and Pharmaceutical industries account for 5.5% of FDI in health care; External commercial borrowings: the government has decided to permit entities in the hotels, hospitals and software sectors to avail ECB up to 100 million USD per financial year, under the automatic route, for foreign currency and/or rupee capital expenditure for permissible end use107; Private equity investments in the healthcare sector amounts to 749 million USD across 25 deals in the first half of 2012, as against 421 million USD and 498 million USD during the same period in 2010 and 2009 respectively. The fund brings in not only the capital but also the adequate strategic planning and management skill sets for growth; Individual investors; Foreign institutional investors like AIG, BUPA, and Allianz which have entered into a JV with Indian companies to invest in the private health insurance market in the country, catering to the urban

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107 [https://rbi.org.in/SCRIPTs/BS_ViewMasCirculardetails.aspx?id=9840](https://rbi.org.in/SCRIPTs/BS_ViewMasCirculardetails.aspx?id=9840)
population; Venture capital funds; public Private partnership and Other sources like many international donor organizations like Bill & Melinda Gates Foundation, Clinton Foundation, USAID etc. For example, the current operational plan of DFID (2011-15) expects the UK to contribute 173 million GBP on education and 248 million GBP on health related activities in India during the period from 2011 to 2015.

Implementing Technology Innovations

E-Health Initiatives

E-Health Projects planned/implemented like Integrated Disease Surveillance Project, Tele-ophthalmology project, National Telemedicine Grid, National Onconet Project, National Medical College Network, National Digital Medical Library Consortium, SAARC telemedicine network, Pan-African e network project.;

Telemedicine Projects being implemented by Indian Space Research Organization (ISRO), Dept. of Information Technology, Ministry of Communication & IT, Ministry of Health & Family Welfare, State Governments and Medical Institutions Education & Training towards Capacity Building with several training programs in this field which include Apollo - Anna University, Chennai (certificate course); School of Telemedicine and Biomedical Informatics Telemedicine, SGPGIMS (structured courses); Hospital Information System, Biomedical Informatics, Medical Multimedia and Image management, Medical Knowledge Management, Artificial Intelligence, Virtual Reality and Robotics

Initiatives for Increased Quality and Follow-up in Healthcare:

Information Systems and Registers: Current developments include an expansion of hospital-based cancer registries to look at patterns of care and survival, bringing in more details on cancer cases affecting three sites; breast, head & neck, and cervix.

Healthcare Technology Laws and Regulatory Compliances in India: Presently the healthcare industry and healthcare entrepreneurs of India are acting more on the side of violation than compliances.

Recommendations on Electronic Medical Records Standards have been prescribed that have to be followed and complied with by Indian clinics and healthcare professionals of India.

Pricing of Drugs: In rural India, the share of drugs in the total OOP is estimated to account for nearly 83%, while in urban India, it is 77%. The share of drugs in the total inpatient treatment in rural and urban India is around 56% and 47% respectively. At present, only 76 drugs, accounting for one-fourth of the total drug market in terms of value are price controlled. Finally drug retail margins

108 E-Health Initiatives in India; (file:///C:/Users/Nisha%20Arora/Desktop/Official/WHOI%20APW%202014/References%20for%20element%204/e-Health%20Initiatives%20in%20India.pdf, accessed on 31st Jan, 2015)
110 http://perry4law.org/cyberlawsinindia/?p=93
111 http://mohfw.nic.in/WriteReadData/I892s/2857975681461059607.pdf
are extremely high in the pharmaceutical market. Department of Pharmaceuticals notified the New First Schedule of DPCO, 2013 based on National list of Essential Medicines (2015) on March 10, 2016. NPPA has started the exercise of fixing the ceiling prices of the medicines in the NLEM-2015 and in a short span fixed and notified the ceiling price of 330 formulations as on June 10, 2016. The NLEM 2015 contains a total of 799 formulations under 30 therapeutic groups. NPPA is working to fix the price of these drugs as soon as possible. As on date, 969 scheduled formulations are under direct price control[112].

Medical devices: The Mashelkar Committee y recommended the creation of a specific medical devices division within the CDSCO in order to address the management, approval, certification and quality assurance of all medical devices. The Drugs Consultative Committee approved these recommendations in 2005, ensuring that in future all devices would be licensed for manufacture, distributed and sold by the CDSCO, with special evaluation committees in order to ensure that the concerned manufacturing units complied with the requisite GMP requirements[113].

Biotech Products: The Ministry of Environment and Forests under the Environment (Protection) Act of 1986 have notified the rules for the manufacture, use, import, export and storage of hazardous microorganisms or genetically engineered organisms or cells. As per these rules, biological materials are regulated from the R&D stage to their release in the environment.

Clinical Trials: The conduct of clinical trials in India has been critically reviewed at national and international platforms An expert committee under Dr.Ranjit Roy Choudhry constituted by the Ministry of Health and Family Welfare to formulate policy, guidelines and standard operating procedures for approval of new drugs including biologicals, clinical trials and banning of drugs was announced on 6th February 2013. Based on the recommendations the Central Drugs Standard Control Organization (CDSCO) in India has now recently made an amendment to schedule Y of the Drug and Cosmetic Act The major amendments are related to the reporting of serious adverse events (SAEs), compensation to study participants in case of death or injury, responsibilities of different stakeholders involved in the clinical trials, regularization of the Ethics Committees and make them accountable for the clinical trials they approved. All the stakeholders now have added responsibilities and accountability.

Promoting competition to improve availability and affordability of health products consistent with public health policies and needs: The Competition Act 2002 aims to prevent practices having an adverse effect on competition and abuse of dominance of enterprises either by entering into Healthcare sector is distinct from other sectors in that there exists an inherent asymmetry of information that renders it difficult for the sector to compete in the manner that other sectors do. Since competition does not affect the healthcare sector the way it does other sectors there is a need to devise a mechanism to ensure identification of such issues[114,115,116,117,118].

112 http://www.nppaindia.nic.in/
113 http://cdsco.nic.in/Medical_div/Final%20Guidance_Doc_Form-28_31-10-2012.pdf
114 Chatterjee, S. "Regulatory changes in conduct of clinical trials: A need for review." Indian journal of pharmacology 45.4 (2013): 323
India’s healthcare sector needs to scale up considerably in terms of the availability and quality of its physical infrastructure as well as human resources so as to meet the growing demand and to compare favourably with international standards. The priorities for government for healthcare must be such it covers the three basic objectives: Affordability, Reach and Quality of services.

**Element 7 Ensuring sustainable financing mechanisms for R&D in health**

Financing health R&D in India

In the past decade the funding available from various Indian government agencies has been complemented with funding from The Bill Melinda Gates Foundation, Wellcome Trust, US-NIH etc. in order to accelerate the R&D process from basic and applied research through clinical trials and initial manufacturing India. In addition, partnerships with several institutions has been established in the US, in EU and Australia to learn from their best practices. The government can play a major role in shaping innovation system by directly funding high value research that would otherwise not be undertaken by private businesses. Innovation is critical to India’s growth and its preparedness for meeting emerging economic social and environmental challenges. There is a need for new thinking about how to channelize this investment such that the private sector is encouraged to get involved and the global innovation enterprise is more responsive to the needs of the poor.

In recent years in India agencies like BIRAC have been created that provide better incentives to biotechnology industry to investment in product development for diseases of importance to India and the region., It has played a crucial role in consolidating the strengths of biotech start-ups, small and medium sized industry, where innovation actually takes place; has successfully promoted PPP in diverse forms and has directed the energy towards public good. In summary they have created a mechanism where innovation in small and medium sized industry is promoted by absorbing part of their risks using public funds.

Evaluation of impact assessment of two largest public funded programs in India namely the Small Business Industry Research Initiative (SBIRI) and Biotechnology Industry Partnership Program (BIPP) suggests that these programs focus on small, new high growth firms that are capable of creating employment. These have focus on high risk and support projects that involve high quality research and have the potential and are instrumental in IP creation. The funding schemes have had positive

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116 Competition Law in India”, Abir Roy and Jayant Kumar, Eastern Law House, 2008.
119 Robert Hecht; Paul Wilson& Amrita Palriwala. Health Affairs; 2007. 28(4) 974-985:10.1377/hlthaff.28.4.974

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effects for the beneficiary firms in terms of employment and sales growth; provide a bridge between universities, research laboratories and businesses and have a “crowding in effect”.120

Gaps in the current funding system in India are inadequate volume of R&D funding; lack of flexibility in the funds; absence of processes and norms for quick regulatory approvals. To overcome these some promising new mechanisms of sustainable funding for early discovery are milestone based prizes which could be an effective mechanism to stimulate discovery in order to replenish the product development pipelines to ensure a continued flow of promising candidates into late-stage development.121 Prizes could be a way to test important features, such as IP management and access provisions, of more ambitious and potentially transformative prize mechanisms, including final product prize funds that would reward innovation in proportion to health benefit.122

Product development and access for use in developing country like India should be insulated from shifts in donor circumstances and priorities. For this the countries have to develop sustainable financing mechanisms from sources within the country. The UNITAID airline ticket tax and the “voluntary solidarity contribution” being developed by the Millennium Foundation are promising examples of sustainable funding sources. Taxes on financial transactions, particularly a small tax on currency exchange, are another potentially promising way to raise long-term funds for neglected health R&D as well as for other development priorities.123

**Taxation on tobacco products** is another way of sustainable source of revenue generation for the governments for addressing other priorities. For example for vaccines, **GAVI** is the logical source of funds for purchase of vaccines. For drugs and diagnostics for AIDS, TB, and malaria, the **Global Fund and UNITAID** provide this assurance, including crucial technical and financial support during the WHO Prequalification process. A “revolving fund” like that of PAHO could be another option for support of access to such products. Hand holding during late-stage product development and activities related to delivery would be a logical extension of any of the funds needed to improve access, enabling it not only to fill critical gaps in the portfolio of products that it supports, but also to influence product design and cost, and to build in support for critical phases of registration, for funding gathering of data to build evidence for introduction purchase, and delivery.124 Some examples of Public Private Partnership based R&D programmes in India are Startups and MSMEs (PRISM) scheme, Building Industrial R&D Promotion Programme (BIRD), Patent Acquisition and

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120 Aradhana Aggrawal and Sakshi Chawla “Promoting innovation through Private Public Partnership: An assessment of SBIRI/BIPP programs. Wadhwani Foundation


125 DNDi: Financing neglected disease R&D: principles and options, March 22, 2010
Collaborative Research and Technology Development (PACE) scheme, Technology Development and Demonstration Programme (TDDP), Drug and Pharmaceuticals, Technology Development Board, Cluster Innovation Centre’s, India Inclusive Innovation, Multiplier Grant Scheme, New Millennium Indian Technology Leadership Initiative (NMITLI), Technology Information, Forecasting and Assessment Council (TIFAC), Biotechnology Ignition Grant (BIG), Contact Research and Services (CRS), Small Business Innovation Research Programme of India (SBIRI)\textsuperscript{126}\textsuperscript{127}, Biotechnology Industry Partnership Programme (BIPP) – An Advanced Technology Scheme (ATS)\textsuperscript{128}, DBT and Bill Melinda Gates foundation, University Innovation Cluster

Few examples of Indian Biodesign Innovation Initiatives are Centre for International Biodesign Alliance (Stanford-India Biodesign), Centre for Biodesign and Diagnostic (THSTI, ICGEB, AIIMS and University of Turku), Health Technology Innovation Centre (Indian Institute of Technology Madras and Department of Biotechnology), Bio-design Engineering Initiatives (IISc Bangalore and Department of Biotechnology (DBT)), National Bio-design Alliance, Stanford India Biodesign (Department of Biotechnology, Ministry of Science and Technology, Government of India, Stanford University)\textsuperscript{129,130,131,132}.

**Element 8: Establishing Monitoring and Reporting Systems**

Monitoring & Evaluation of health research programs is an important element to find out the progress and feasibility of the same. Low and middle income economies in the world have very limited resources and subsequently, the spending on health systems is less than 1% of GDP.

The major health programs are evaluated through national sample surveys and census survey data\textsuperscript{133}. Hence the remedial measures as well programs modification and implementation for communicable and non-communicable diseases is long process in the current situation. These census takes place once in a decade and hence getting the real time data of the populace is an issue. National Sample survey and District Health surveys have limited mandate to evaluate and monitor

\begin{itemize}
\item \textsuperscript{127} Aradhna Aggrawal and Sakshi Chawla “Promoting innovation through Private Public Partnership: An assessment of SBIRI/BIPP programs. Wadhwani Foundation
\item \textsuperscript{129} Stanford India Biodesign: http://www.stanfordindiabiodesign.in/home/redirect/CIBA - VH7jF1eUckg
\item \textsuperscript{130} http://biodesign.stanford.edu/bdn/news/annualreports/2013BiodesignAnnualReport.pdf
\item \textsuperscript{131} http://biodesign.stanford.edu/bdn/news/annualreports/2013BiodesignAnnualReport.pdf
\item \textsuperscript{132} http://biodesign.stanford.edu/bdn/global/sourcebook/India-Overview.pdf (accessed Nov 2014)
\item \textsuperscript{133} http://www.who.int/bulletin/volumes/94/4/15-158493/en/
specific programs in accordance to decision by respective ministries covering a small representative sample.

The capacity of medical colleges in particular and the health sector have increased but so has the population which has impacted the development activities negatively. Hence dynamic monitoring and evaluation is the need of the hour\textsuperscript{134}. The lowest economic quartile of the society always remains out reach of the health programs which needs to be thoroughly investigated\textsuperscript{135}.

The health system priorities identified are support the strengthening of health system; preparedness, surveillance and response and corporate services/enabling functions. As per the national priorities several programs have been initiated which have integrated monitoring mechanisms generating yearly annual reports. Such as Human Immunodeficiency Virus Infection/Acquired Immunodeficiency Syndrome(HIV/AIDS) - Department of AIDS Control, Revised National TB Control Programme (RNTCP) ,National Vector Borne Disease Control Programme (NVBDCP), Integrated Disease Surveillance Project (IDSP), National Leprosy Eradication Programme (NLEP), Pulse Polio Programme:----Immunization programs have been success ( India Polio free; 2013), Universal Immunization Programme (UIP), National Mental Health Programme (NMHP), National Programme for Prevention and Control of Deafness (NPPCD), National Programme for Control of Blindness (NPCB) and National Action Plan & Monitoring Frame work for prevention and control of NCDs (2013-2020) from MoH India.

A new approach towards Integrated disease surveillance programme is a major component of monitoring. The surveillance activities that are well developed in one area may act as driving forces for strengthening other surveillance activities, offering possible synergies and common resources. For example, Integrated Disease Surveillance Project (IDSP) ,launched with World Bank assistance in November 2004 to detect and respond to disease outbreaks . The project was extended for 2 years in March 2010. From April 2010 to March 2012, World Bank funds were available for Central Surveillance Unit (CSU) at NCDC & 9 identified states (Uttarakhand, Rajasthan, Punjab, Maharashtra, Gujarat, Tamil Nadu, Karnataka, Andhra Pradesh and West Bengal) and the rest 26 states/UTs were funded from domestic budget. The Programme continues during 12th Plan under NRHM with outlay of Rs. 640 crore from domestic budget only\textsuperscript{136}. A network of microbiology laboratories (Indian Network for Surveillance of Antimicrobial Resistance - INSAR) at premier medical colleges and hospitals in India was formed with support from the World Health Organization. The network aims


\textsuperscript{135} Ref : Countdown to 2015

to monitor antimicrobial resistance and to review the magnitude of its problem in India. Initially, a few organisms of public health importance have been chosen for monitoring their prevalence and antimicrobial resistance patterns, with *S. aureus* being chosen among the Gram-positive organisms.

A Network of Viral and other Infectious Disease Diagnostic Research laboratories is being set up in the country by ICMR and DHR to build capacity for handling outbreaks and carry research of all emerging-re-emerging and common viral diseases as well other infectious diseases like tuberculosis. One BSL IV, Asia’s first laboratory for Human Medicine established at NIV, Pune to deal with most dangerous lethal infections like hemorrhagic fevers, agents of bioterrorism etc inaugurated 28th December, 2012. International Collaborations like EVAL-HEALTH which is a project funded by the Seventh Framework Programme of the European Commission which aims to support monitoring and evaluation of health research and to help develop understanding of the role of evidence in public health and health systems.

The R & D is an important part of the health sector and more so in the area of pharmaceutical sector without which the sector cannot thrive and develop. Commission in Intellectual Property Rights, Innovation and Public Health (CIPIH) had postulated that in the context TRIPS Agreement, it was expected that after implementation, investment by multi-national corporations (MNCs) would rise in India to give impetus R & D. But the actual scenario is quite different. Indian companies who initially had an advantage in the production of generic drugs mainly through the process of reverse engineering might find it difficult for the discovery of new products and perform well in the pharmaceutical sector. There are no incentives for MNCs to introduce R&D in Indian markets which are price sensitive for any innovation i.e drugs, diagnostics vaccines or medical devices. In the patent regime era providing cheap generic drugs for the economically poor remains a challenge unless development and manufacture is increased dramatically in the lesser developed economies.


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