THE GRADUATE INSTITUTE | GENEVA
GLOBAL HEALTH PROGRAMME

HARVARD Global Health Institute

EVENT WORKING PAPER 1

PRIORITY SETTING FOR HEALTH R&D

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GLOBAL HEALTH PROGRAMME | 2013

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Event Working Paper 1:
Priority Setting for Health R&D

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I. Introduction

This discussion paper has been prepared for participants attending a workshop at the Graduate Institute in Geneva on 24 April 2013 to explore ideas for securing collective action towards a credible platform for monitoring, coordinating, and financing research and development (R&D) for the health needs of people living in low- and middle-income countries. The workshop will divide into two streams for intensive discussions: one dealing with **governance** issues while the other examines **priority setting** approaches.

In the accompanying Background Paper 2, we describe potential governance approaches to implement demonstration projects, as requested in the draft resolution which will be discussed at the 66th World Health Assembly (WHA) in May 2013, and how they can be scaled up into a sustained, long-term solution. Paper 2 draws on experiences from international cooperation across health, environmental, and agricultural sectors and examines what the global system for health R&D can learn from them. It then provides a list of questions to lead the workshop discussions in exploring scenarios for creating a global R&D platform.

Within the platform that is eventually chosen by the global community, it will be necessary to engage in prioritization processes to decide how best to use the available R&D resources. In the present Background Paper, we summarize the need for and some potential approaches to priority setting processes; consider the attributes of one option presented as an example of priority setting; and provide a list of questions to lead the workshop discussions in exploring scenarios for R&D priority setting.

II. Background

The need for a coordinated global process for priority setting

A large and diverse array of actors provide resources for global R&D for health, which by 2009 had risen to US$ 240 billion per year[1]. Most resources directly fund the performers of research, development and innovation, but a small fraction is passed to intermediaries which focus

attention on and channel funding to neglected areas. The overall result is the creation of products, process and knowledge relating to both technological and social areas of innovation - some generated in the private sector and governed mainly by commercial interests, while some take the form of global public goods (GPGs), mainly generated in the public sector. The entire system operates in an external environment of drivers (economic, political, social), incentives and motivations (financial, humanitarian, scientific, human), promoters (science and technology policies and investments, legal and commercial frameworks for innovation) and barriers (restrictions in access to trade and markets, knowledge, investment funds, technologies) as well as being subject to positive and negative feed-back mechanisms that operate between various elements.

While this global health research and innovation system [2] has delivered considerable knowledge and many pharmaceuticals valuable for the treatment of diseases of importance in high-income countries (HICs), it has manifestly failed to address many health conditions predominantly found in low- and middle-income countries (LMICs). Efforts to overcome this failure have included a series of initiatives to consider how to organize and finance R&D for Types III diseases (for which the burden lies overwhelmingly or exclusively in poor countries) and Type II diseases (for which the predominance of the burden lies in poor countries) and for some Type I diseases (for which the burden is similar in poor and in rich countries)[3], the most recent involving the WHO's Consultative Expert Working Group [4], whose report is being discussed by the WHA in May 2013.

Whichever governance model is ultimately adopted by the global community, it will provide a framework of agreements concerning the financing and coordination of health R&D and will set some boundary conditions concerning what kinds of diseases or targets are to be addressed. Within the chosen framework, it will then be necessary to select the specific diseases or targets and to determine which kinds of research are needed (along the innovation pathway through basic, applied, drug development, pre-clinical, clinical and implementation research), assigning priorities based on a set of criteria that need to be established. As indicated in the accompanying Background Paper 2, it is possible that the entire global programme may be implemented in successive phases, potentially with a first phase involving demonstration projects and later expanding into a full implementation phase with a wider scope – in which case the selection criteria, and even the selection methodologies, for prioritization may need to be varied over time.

To attract widespread support and legitimacy, the process for coordinated priority setting for R&D to address diseases predominantly or exclusively affecting poor populations will need to be recognized as efficient, equitable, transparent and participatory, designed and implemented

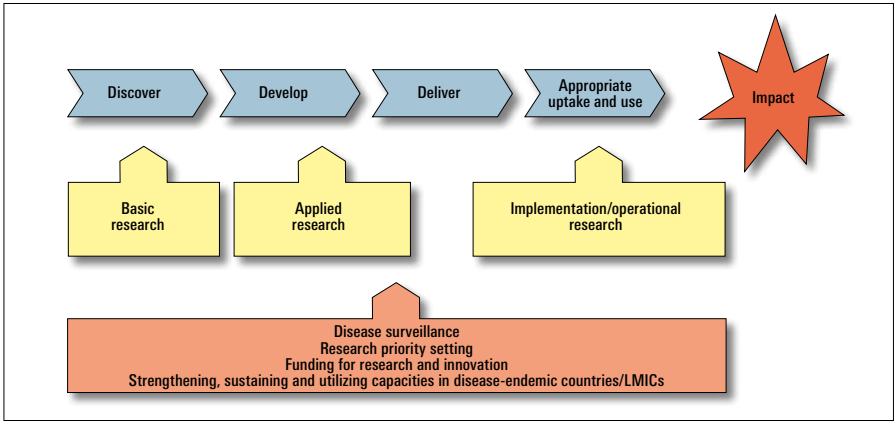
in the context of understanding the overall global health research and innovation system and the many factors within it that must contribute to the choosing of priorities.

The R&D pipeline

The R&D pipeline producing medicines to prevent and treat diseases is illustrated in Box 1. All stages, from discovery to uptake and use, are essential if a new product is to have impact on the health of the target population and research is essential at each of these stages to ensure safety, efficacy, practical utility and positive benefits in terms of health and health equity. A **spectrum of different types of research** is involved along the pipeline – research differing markedly in the locations where it is conducted, the types of researchers and research methodologies, the order of magnitude of funding required and the types of funders who support the work. A variety of factors contribute to the impetus for movement along the pipeline, including the recognition of changing disease patterns, prioritization of targets, evolving funding mechanisms for research and innovation and policies to stimulate and support the strengthening, sustaining and utilization of R&D capacities in disease-endemic countries and in LMICs generally.

While noncommunicable diseases (NCDs) are now a global problem, the importance of including NCDs as well as communicable diseases in the discussion becomes evident when the constraints that are faced by LMICs are considered. Local factors that can limit the use of available treatments for NCDs in LMICs include: purchase/running costs; workforce shortages (doctors, nurses, technicians); and maintenance costs of equipment for diagnosis and treatment. Consequently, the issues of whether a particular health technology is affordable and applicable in the local setting are especially important, and in this context it is valuable to adopt the concept of **'frugal' technologies**[5]. These are technologies that are designed from the outset with the objectives of reducing costs, reducing complexities in use; and expanding utility in challenging settings (e.g. environment; poverty). Furthermore, in an era when healthcare costs are spiralling everywhere and the health system of virtually every country in the world is struggling to keep up, it is evident that the concept of frugal technologies is not just relevant to LMICs but is one that has universal significance: ideally, all technologies for health, including drugs, equipment and devices, should be designed to be 'frugal'.

Box 1: R&D pipeline for medicines to prevent and treat diseases



Objectives of priority setting

Given the complexity of the global health research and innovation system and the range of unmet health needs to be addressed, it is necessary to develop a coordinated, evidence-informed process for priority setting (Box 2) that meets a number of objectives:

- The primary objective will be to ensure that new drugs, vaccines and diagnostics which are needed to treat diseases prevalent in LMICs are developed and that the products are safe, effective, affordable and suitable to the conditions in which they will be used, thereby contributing to better health and health equity globally.
- Secondary objectives could include:
  - avoiding unnecessary duplication of effort;
  - avoiding waste of funding;
  - encouraging equity-enhancing investments;
  - enabling priority efforts to be directed to urgent or neglected areas by:
    - assisting policy makers and funders in setting and management of global priorities
    - assisting policy makers and funders in selecting the most productive areas for attention along the innovation pipeline (e.g. where there is insufficient priority for specific areas of basic science, inadequate funding for lead uptake and product development, or lack of funding or capacity for clinical trials at appropriate locations; or where competing product development pipelines within and between specific diseases necessitate choices to be made);
  - facilitating cooperation between public and private sector actors;
  - promoting inclusion of a wider range of actors in the R&D process – e.g. ensuring involvement of LMIC researchers in developing solutions to problems in their own countries; and/or R&D capacity building in LMICs.

Box 2: Evidence-informed priority setting

> The explicit and rational setting of priorities for investment in research is now accepted as an integral part of any research management process. Setting priorities in research can serve to act as a catalyst for public debate, for bringing together different stakeholders, and for creating networks. These networks would ideally comprise researchers in the public and private sectors, decision-makers in governments, and civil society. Most importantly, the very act of priority setting can provide valuable direction for the allocation of public and private research funds into areas of strategic importance.
>
> Source: Priority-Setting Methodologies in Health Research; 2008, WHO[6]

Systematic approaches to priority setting

At present, there is no global coordination of R&D for communicable and noncommunicable diseases of poverty – either in terms of governance or priority setting. The field is highly fragmented, with most actors working either in isolation or as a part of small groupings or networks involving a limited sub-set of entities with shared goals. Thus, there are partial and temporally limited efforts to coordinate selected aspects of the overall global health research and innovation system and prioritisation of elements of the innovation pipeline discussed above. These can be regarded as valuable/realistic models in their own right, as embryonic forerunners of a comprehensive coordination mechanism, or as sources of learning about the limitations of incomplete approaches[7].

The 1990 report[8] of the Commission on Health Research for Development noted that *"too often priorities for public sector health research and development investments are determined with little concern for the magnitude of the problem to be addressed, for the extent to which scientific judgment supports the possibility that new products and initiatives will be more cost-effective than available alternatives, or for ongoing efforts elsewhere"*.

Subsequently, systematic approaches that have been developed to assist priority setting include:

- The Commission on Health Research for Development advocated the use of a systematized approach to priority setting within a country's Essential National Health Research strategy and the Council on Health Research for Development (COHRED) assisted LMICs with the implementation of this approach. Three essential stages were recommended by COHRED[9] to increase the effectiveness of the priority setting process: (i) Planning, involving

identifying leadership and stakeholders and gathering and analysing relevant information; (ii) Setting the priorities, involving preparation of the information in a useful form and determining the process and weighting methods for selecting priorities; (iii) Implementing the priorities, involving translating them into research portfolios and incorporating them into research programmes that are invested in and periodically updated.

- The WHO Ad Hoc Committee on Health Research developed a five-step methodology [10] involving assessing a set of factors linked to the public health dimension: magnitude of burden of disease, determinants (risk factors), level of knowledge in relation to interventions, cost-effectiveness and resources.
- In order to incorporate 'actors' as well as 'factors', the Global Forum for Health Research [11] added a second, institutional dimension to the public health dimension, in a tool known as the 'Combined Approach Matrix (CAM)'. The institutional dimension increased the analytical power of the tool by allowing each of the public health elements to be analysed according to four institutional levels, namely the individual, community and household; the health sector; all other sectors; and governance.
- The tool was further refined into a Three-Dimensional Combined Approach Matrix (3D CAM) to capture the multiple forms of discrimination, marginalization and vulnerability which operate beyond the original two dimensions and to ensure that the priority setting in research benefits those with greatest need and contributes to improved health and equity [12]. This extension of the original CAM emphasises the context within which the priority setting takes place and the values that are explicitly or implicitly incorporated in the process.

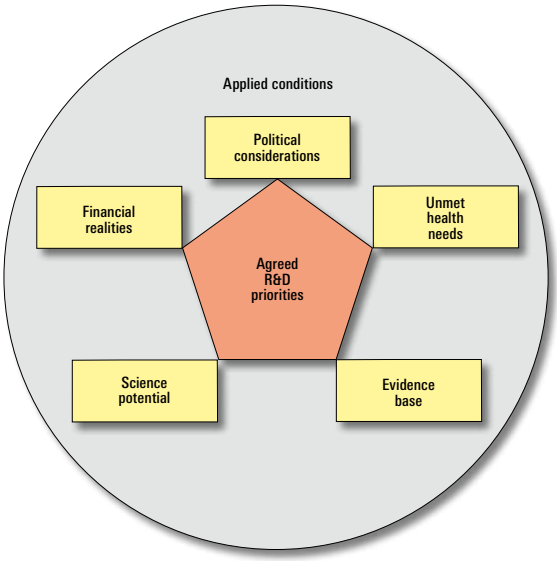
III Proposal of an option for coordinated priority setting of R&D for diseases of the poor

To assist the debate on how a globally coordinated priority setting process for R&D for diseases of the poor could be constructed and operated, one **possible option** is offered here. This attempts to incorporate the many factors and forces that need to operate in the selection of priority R&D that should be coordinated and funded. It is offered in the hope that it will stimulate close inspection and debate, identifying its strengths and weaknesses so that it can be either improved and considered for adoption by the international community, or replaced by an alternative model that has clearly superior features.

Factors in priority setting

A major challenge is to set out clearly a process for priority setting that, if adopted, would be widely accepted as fair and balanced – that meets the perceived priority needs of poor populations while satisfying the requirements for scientific rigour and for incorporating political and financial realities; and that takes account of any over-riding conditions that need to be applied, such as in-built values (e.g. equity orientation; cost effectiveness; restrictions to certain types of diseases and conditions).

Box 3: Factors to be considered in setting priorities for health R&D for diseases of the poor



In practice, there are at least five groups of factors that need to be taken into consideration, in addition to any over-riding conditions, summarised in Box 3. Each of these defines relevant groups of actors who need to be engaged in the selection and prioritisation of R&D targets:

- **Unmet health needs**
  Sources should include burden of disease, Demographic and Health Surveys, reports from NGOs and from civil society groups, including the affected communities.
- **Evidence base**
  Scientific input on what is known about the nature of the disease; and about currently available treatments and their problems, limitations and disadvantages.
- **Science potential**
  Scientific input on the potential for developing new/better treatments designed specifically for the relevant populations – taking account of affordability, ease of use, potential for access ('frugal' technologies) and realistic scenarios of approaches with estimates of timescales and pathways to bring treatments to patients.
- **Financial realities**
  Realistic estimates of cost per annum and timescale to bring treatments to patients.
- **Political considerations**
  Prioritisation is, in its ultimate stages, a political process involving choices among a number of options that are all individually, in principle, desirable. The selection of 'best buys' cannot only be left to technical experts to decide on the competing claims of different groups for remedies to alleviate their suffering – there must also be a recognition of political factors. These may include the political urgency of meeting international commitments (e.g. Millennium Development Goals; International Health Regulations), global health threats (e.g. pandemics) and national commitments (e.g. political promises made in election campaigns and parliamentary bills) and priorities (e.g. tackling endemic infectious diseases, or regional health problems like Chagas Disease; responding to national advocacy groups on behalf of specific causes of ill-health; redressing long-standing health inequities).
- **Applied conditions**
  A further set of factors is constituted by any applied conditions that are built into the overall system – such as those that might be set in the formulation of the R&D Convention. These might include, for example:
  - Decisions to focus exclusively on Types II and II diseases, or to permit only inclusion of specially recognised sub-sets of Type I diseases.
  - Decisions to exclude areas where there is evidence of strong activity by the private sector; or only include specially recognised sub-sets in these cases, such as where the available commercial products are substantially unsuited for use in resource-poor settings.

→ Decisions on the extent to which research capacity utilization and/or strengthening in LMICs are desirable or essential components of some (a specified proportion?) or all R&D programmes financed.

Structuring multi-stakeholder priority setting

Key actors

At present, components of the effort to address drug development for a particular neglected disease are undertaken in a fragmentary and ad hoc fashion by a number of actors, including WHO, Product Development Partnerships and disease-specific partnerships. The present proposal calls for a series of **Working Groups** to address globally the research prioritisation in each problem area comprehensively and systematically, with commonality in approach between the Working Groups and with an **Oversight Group** able to draw together common needs, identify synergies, summarise the global efforts and make final choices among competing priorities. The structures and compositions of the groups would be designed to address current weaknesses in the existing fragmented approaches, including the paucity of funding for R&D for some 'very neglected' diseases and questions of adequate representation by disease-endemic countries, the private sector and civil society groups concerned with access, community participation and equity issues.

Apportioning responsibilities

To ensure that the process for coordinating and setting priorities for R&D to address diseases predominantly or exclusively affecting poor populations is efficient, equitable, transparent and participatory, **it is proposed that a two-level structure is established**:

→ In **Level 1**, the composition of actors will be predominantly technical, but with some participation by political representatives. The work at this level will result in a report for each health problem under consideration, assessing the unmet health needs, evidence base on the current gaps in treatment, science potential for new approaches and the likely timescales and costings for proposed R&D. As indicated in the operation of the CAM [11,12], incomplete information is not a barrier to taking decisions about priority areas for research (which may include research to close the critical knowledge gaps that have been identified).

Experts and stakeholders from the public and private sectors will be convened in a series of **Working Groups** to identify the research agendas necessary to address pressing health problems, both of global significance and relevant to LMICs. The Working Groups will deal with areas based on:

→ burden of disease and risk factors – e.g. communicable and noncommunicable diseases;

injuries; sexual and reproductive health, mental health, obesity, tobacco, alcohol, substance abuse
- → health systems
- → other determinants of health beyond biological and health systems factors: economic, environmental, political, social

Within each area, the Working Groups would:
- → identify the overall research agenda, considering the entire research and innovation chain from idea to impact
- → prioritise the most critical areas for action along a temporal pathway
- → estimate additional required expenditure
- → propose a monitoring mechanism to overview progress
- → propose reporting and communication mechanisms to enable the actors to keep abreast of developments

→ In **Level 2**, the composition of actors will be predominantly political representatives, but with some participation by technical representatives. The work at this level will result in establishing a prioritised list of R&D programmes that are considered the best choices for funding.

An **Oversight Group** will conduct the Level 2 actions and will fulfil two primary roles:

1. Decide on the areas in which Working Groups are to be constituted to conduct the priority setting processes. This could be based on proposals originating from among the members of the Oversight Group itself; external proposals arising in an unsolicited manner; and/or through an open call to the global community.
2. Assemble the composite picture provided by the Working Groups across the different areas. The Oversight Group's deliberations will consider the competing options and result in establishing a prioritised list of R&D programmes, taking full account of political, humanitarian and financial circumstances and any in-built applied conditions. There can be flexibility in what the final 'priorities' would look like and the list may not need to be fully ranked, but might, for example, define, eg 10 promising projects that all should be funded.

Once priority R&D has been selected, two options exist for the organization of processes to make the allocations of the work – and associated resources – discussed above:

→ In **Option 1**, the combination of Working Groups and Oversight Group take the lead role in identifying suitable actors and sites for the conduct of the R&D. This model (which is similar to the way that Task Forces in the Special Programmes TDR and HRP at WHO have operated) may be considered efficient on the grounds that these groups, having been intimately engaged

in the identification of needs and opportunities, are intensely knowledgeable about the best places to conduct the work. However, this may also be considered to generate conflicts of interest, with the prioritising groups potentially benefiting in some way from their own decisions. It is highly preferable that there be an independent mechanism for commissioning or incentivizing research using the different tools available (as in Option 2), to avoid a process that can be seen as anticompetitive and may result in conflicts of interests.

→ In Option 2, the identification of suitable actors and sites for the conduct of the R&D is made independently by a **Secretariat specially established to manage the whole process** – from the organization of the composition and work schedules of the different groups involved in prioritization to the advertising or commissioning of research activities, distribution of resources, collection of research reports and monitoring and evaluation of the entire programme. To avoid capture or internal bias, the Secretariat could operate and manage a competitive process involving independent external reviewers. The Secretariat would be overseen by whichever top-level governance mechanism is selected.

IV R&D demonstration projects to address identified gaps that disproportionately affect poorer countries

Among other recommendations, the Open-Ended Meeting of Member States [13] organized by WHO in November 2012 called for immediate work on a few health R&D demonstration projects to address identified gaps that disproportionately affect poorer countries.

This could be regarded as a stand-alone activity to provide some 'quick wins' while countries continue to debate the merits of global coordination and financing mechanisms for health R&D. However, it could also be used, in part, to provide a demonstration of key elements of the more comprehensive, global coordinated priority setting process.

In addition to this issue of the overall purpose of conducting a few health R&D demonstration projects, a further key consideration relates to the mechanism(s) that should be used to identify candidate projects and to make the selection from among them of those to be conducted. One hand, the generation of the entire candidate list should ideally be the result of some well-designed, evidence-based and participatory process (for example, it could be run as a pilot version of the model proposed above in Section III). On the other hand, some preliminary suggestions for possible high-priority areas that would attract strong and widespread scientific and political support may be extremely valuable to help galvanise action by the global community.

V Conclusions and questions for consideration

The Workshop session will focus on two aspects:

- Models for coordinated priority setting
- Demonstration projects to address identified gaps that disproportionately affect poorer countries

Participants in the Workshop on Priority Setting will examine the options for coordinated priority setting and consider a number of questions:

Question Set 1:

Regarding the option for coordinated priority setting outlined in this paper:

- To want extent is the option realistic and feasible?
- What are its key advantages and disadvantages as a mechanism for global priority setting?
- Within the broad boundaries of the concept, how could this option be refined and improved?
- What are considered to be the key organizational and political hurdles that would need to be overcome to obtain support for the implementation of this option?

Question Set 2:

Considering alternative options that might be used, that are substantially different from the one outlined in this paper, to operate coordinated priority setting for global health R&D for diseases of the poor:

- What are the main distinguishing features of each alternative proposed and to want extent is each such alternative realistic and feasible?
- What are its key advantages and disadvantages compared with the option offered in this paper?
- What are considered to be the key organizational and political hurdles that would need to be overcome to obtain support for the implementation of the alternative option(s) proposed?

Question Set 3:

Regarding the selection of demonstration projects to address identified gaps that disproportionately affect poorer countries, consider:

- The desirability of focusing the selection of the projects exclusively around the objective of providing some 'quick wins' which will benefit global health by ensuring the development of needed treatments for neglected diseases; versus the option of incorporating additional

criteria which would also provide a demonstration of key elements of the more comprehensive, global coordinated priority setting process.

- → The mechanism(s) that should be used to identify potential demonstration projects and to select those to be conducted.
- → Ideas for highly attractive candidates for selection that would be most likely to attract broad international support.

At the conclusion of the Working Group discussions, a designated Chair and Rapporteur from each group will assemble a summary report. They will also be responsible for providing a more detailed report of their group's discussions within a few days after the meeting.

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