WHO Stakeholder consultation related to WHA 75.8:
"Strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination"
Introduction and discussion questions

I. Introduction

The WHO Secretariat is organizing stakeholder consultations as instructed by WHA 75.8 "Strengthening clinical trials[1] to provide high-quality evidence on health interventions and to improve research quality and coordination"

The first action for the WHO secretariat is as follows:
(1) to organize, in a transparent manner, stakeholder consultations, in line with the Framework of Engagement with Non-State Actors, with Member States, nongovernmental organizations including patient groups, private-sector entities including international business associations, philanthropic foundations and academic institutions, as appropriate, on the respective roles of the WHO Secretariat, Member States and non-State actors, and to identify and propose to Member States, for consideration by the governing bodies, best practices and other measures to strengthen the global clinical trial ecosystem, taking into account relevant initiatives where appropriate.

While the resolution does not define "clinical trials ecosystem" the secretariat is using the following definition of the clinical trials ecosystem based on the wording of the resolution: the clinical trials ecosystem is the sum of all elements required to fund, prioritize, design, conduct, monitor and report scientifically and ethically appropriate, well-designed, and well-implemented clinical trials as well as features necessary for oversight and coordination.

Such trials should generate high quality scientific data and evidence that inform the scientific state of the art as well as both regulatory decision-making and clinical guidelines processes related to new or existing interventions including through comparative effectiveness, and cost-effectiveness studies. The resolution states that, "clinical trials on new health interventions are likely to produce the clearest result when carried out in diverse settings, including all major population groups the intervention is intended to benefit, with a particular focus on under-represented populations." The elements of the ecosystem may include but are not restricted to: regulations and legislation governing the suitability of data generated for regulatory assessment by national regulatory authorities as well as oversight by research ethics committees; infrastructures as well as institutional and individual research competencies required to implement trial procedures appropriately; systems and personnel to manage, analyse and share data securely respecting national regulations; procedures to report results promptly with a focus on transparency and, increasingly, procedures to share underlying trial datasets once patient de-identification and anonymization have occurred.

Other ecosystem elements include the availability and method of deployment of financial resources, whether from the private or public sectors, to conduct clinical trials and how these are allocated; clinical trials networks and prioritization processes to identify research questions,

[1] "WHO defines a clinical trial as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials may also be referred to as interventional trials. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc. This definition includes Phase I to Phase IV trials." WHO ICTRP.

populations, interventions, comparator groups, and outcomes to be addressed in well-designed trials. Coordination between different elements forms part of the ecosystem. The unmet health needs and disease burden of individuals and populations are related to the ecosystem through the prioritization processes for the utilization of clinical trial structures. The resolution discusses the application of clinical trials in normal times and the need for specific provisions for rapid deployment of clinical trial capacities in times of a WHO-designated Public Health Emergency of International Concern.

Questions for stakeholder consultation:

Introductory question

The following questions go into some detail on elements of the ecosystem, requesting structured inputs.

Before this, we would like to request your overall key inputs on "recommendations for best practices and other measures to improve the global clinical trials ecosystem, taking into account existing initiatives". This may include the role of WHO, Member States and non-State actors. It may also include elements on 1) prioritization of funding and trials, 2) improving quality of the overall evidence generated by the ecosystem including infrastructure, capabilities, standards, governance processes 3) improving collaboration and coordination, and 4) improving translation of results to policies and licensure/authorization. Please share the key elements of your overall input to the submission here.

Question 1

Does the above description capture critical elements of the clinical trials ecosystem? Which elements are missing? Which elements are incorrectly stated? Are you aware of existing up-to-date descriptions of the clinical trials ecosystem relevant to public, private, civil society organisations and philanthropic foundations and all WHO regions? If so, please provide references.

The resolution requests WHO to lead a consultation process to advance best practices and measures that strengthen the global clinical trials ecosystem. The resolution mentions International Council for Harmonization (ICH) explicitly.

Question 2

Are you aware of relevant initiatives besides ICH related to strengthening the global, regional, or national clinical trials ecosystems? If so, please fill out the table below with the most appropriate recent initiatives that may be of relevance and should be considered by WHO in actions related to WHA 75.8. Are there adequate clinical trials networks/initiatives covering all WHO regions and all relevant population groups currently, or are they more or less needed? How can capacity development for clinical trials networks in normal times which focus on endemic communicable or noncommunicable diseases best be related to preparations for future pandemics? How best can mechanisms be put in place to trigger a pivot for activity of endemic disease networks towards pandemic response? What is the role of national vs international networks? How can international networks best meet public health needs in each country they operate in?

Question 3

WHO's R&D Blueprint is a global strategy and preparedness plan that allows the rapid activation of R&D activities during epidemics. What additional steps can be taken to facilitate rapid implementation of agreed trial protocols during pandemics and epidemics?

Question 4
With regard to the resolution text, what do you consider to be "the respective roles of the WHO Secretariat, Member States and non-State actors, [in] … best practices and other measures to strengthen the global clinical trial ecosystem, taking into account relevant initiatives where appropriate"?

The resolution is related to research waste through its focus on best practices for well-designed and well-implemented trials and its wording on preventing underpowered, poorly designed, or under-reported trials.

Question 5
We define research waste for the purpose of this question to be "any practice that does not allow outcomes of research to contribute to science or public health, including poorly designed, implemented or reported research studies". What are the best practices in reducing research waste, and what are the roles of WHO, Member States and non-State actors in implementing such best practices?

The collection, management and sharing of clinical trial data in an ethical and secure manner is fundamental to the conduct and reporting of high quality clinical trials.

Question 6
Many agencies (including WHO) have implemented policies to support data management, sharing and reuse of clinical trials and other research datasets in order to advance science and public health. What measures are needed (legal, technical, other) to ensure that fair and transparent processes are in place to enable access to and reuse of clinical trial datasets in a manner that is appropriate for diverse settings?

Question 7
What do you consider to be measures that can be taken to better utilize digitization and move towards paperless approaches to clinical trials whilst safeguarding subject protections and data quality, measures that are suitable for countries of varying income levels around the world?

Question 8
What measures can be taken, and by whom, to address the insufficient representation of specific population segments in clinical trials, such as low income countries (LIC) and lower middle income countries (LMIC)populations, pregnant and lactating women, neonates, children, the elderly and the immunocompromised?

Question 9
What measures can promote clinical trials that address unmet needs in populations that have been neglected or underserved, such as those suffering neglected tropical diseases, rare diseases, the WHO priority list of antibiotic-resistant bacteria and the WHO R&D blueprint priority list.

Question 10
What measures can be taken, and by whom, to ensure evidence generated from clinical trials is considered higher quality from the clinical guidelines perspective, given that ICH already provides guidance for submission of data to regulatory authorities?

When global research priorities have been agreed, there has been variable success in coordinating funding from research funding agencies to ensure agreed priorities are supported efficiently

Question 11
How can research funding agencies work more effectively together, particularly during epidemics and pandemics? And how best can funding address the inequities in current resource allocations to LIC and LMICs?

ICH is not explored in question 12, given that ICH has a central role concerning National Regulatory Authority (NRA) submissions of clinical data

Question 12
Other than ICH, what critical initiatives relate to the resolution and may already have articulated best practices and clinical trials ecosystems, as framed by the resolution? For example, what is your perspective on clinical trials and the CIOMS Working Group report on clinical research in resource-limited settings? What is your view of the Good Clinical Trials Collaborative guidance?

WHO International Clinical Trials Registry Platform (ICTRP)

Question 13
Given very limited resources, what should be the key priority for improving the ICTRP database, Search Portal and Registry Network to adequately support the clinical trials ecosystem? How can quality of registration data best be improved at both the source registry level and at the ICTRP level to support the aims of the resolution?

The WHO Global Observatory on Health R&D (Observatory) currently provides visualizations of clinical trials globally based on the ICTRP database.

Question 14
What measures can be taken to improve visualizations in the observatory?

Question 15
How can the ecosystem lead to efficient adaptation and deployment of capacities during Public Health Emergencies of International Concern (PHEIC)? Please offer examples of best practices and lessons learned. What do you consider best practices of expedited procedures for rapidly implementing clinical trials in PHEIC that meet regulatory and ethics oversight?

Question 16
If you have any comments, lessons learned, gaps or bottlenecks relating to the clinical trials ecosystem you would like to share, which are not addressed in the previous questions, please provide them here.