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DNDi comments on the zero draft of the WHO CA+ for consideration of the Intergovernmental Negotiating Body at INB4 & 5

February 2023

The Drugs for Neglected Diseases initiative (DNDi) is a not-for-profit research and development (R&D) organization that discovers, develops, and delivers new treatments for neglected patients. Since our creation in 2003 by public research institutions in Brazil, France, India, Kenya, and Malaysia and Médecins Sans Frontières (MSF), we have developed 12 new and improved treatments for six deadly diseases that have reached millions of people utilizing an alternative, collaborative, not-for-profit R&D model.

DNDi welcomes the efforts that the Bureau has made to incorporate the proposals made by Member States and Non-State Actors over the past months. As a not-for-profit R&D organization, DNDi focuses our initial comments on areas where the draft could be strengthened and made more specific to ensure innovation and equitable access to health tools, with a particular focus on conditions on public financing.

As a general comment, throughout the zero draft there are elements which are addressed in multiple places or are separated as a standalone section, for example financing in Article 19, with a lack of clarity about the interlinkages between them. A chapter-by-chapter review misses the opportunity to review these interlinkages. This could be addressed by either addressing such interlinked elements together, or making sure there is a read across chapters. Suggestions of where this is relevant are mentioned below.

Recommendations for Objectives and Vision

1. Addressing inequities in access to health tools should be a central objective

There is now no reference to ensuring equitable access to affordable health tools as part of the objective or vision. Addressing inequities in access to health tools should be a central objective of the WHO CA+. COVID-19 clearly showed that equitable access is the 'unfinished business' of global health and is imperative to 'save lives' as the WHO CA+ aim states.

Suggested Amendment: Article 3 objective(s) should be amended '[ADD Ensuring the discovery, development, availability, and unhindered timely and equitable access to affordable medical and other pandemic response products.]'

Recommendations for Article 9: Increasing research and development capacities

2. The title of Article 9 should be expanded

In addition to strengthening capacity, there is a need to address the limitations and gaps in the way that R&D is conducted and coordinated that have been exposed during COVID-19. To better reflect the need to focus on both aspects, and what is already included under Article 9 in the zero draft, the title of

Article 9 should be amended to read: 'Increase [ADD and enhance/coordinate] research and development [ADD processes] and capacities'

3. Conditions of public financing of R&D should contain more detail

We welcome the reference to the establishment of appropriate conditions on publicly funded R&D. We strongly believe this is where the WHO CA+ can add value in the operationalization of the equity principle. This should remain and the details further developed as part of the negotiation process.

Many aspects of research and development can and should be addressed within the WHO CA+. Some of these elements can be most practically implemented through conditions on R&D financing. The INB processes provide an opportunity to agree upon approaches and conditionalities in advance rather than seek to negotiate during a crisis.

State Parties can and should secure rights on outcomes of research they fund to have the ability to use, license, or assign those rights, if needed, to ensure the development and equitable access to health technologies. They can also attach obligations on recipients to implement specific activities. There can be baseline requirements during inter-crisis periods and others triggered by specific events, e.g., when a public health emergency of international concern (PHEIC) is declared.

Conditions can relate to upstream research collaborations and downstream development collaborations, as well as manufacturing and supply. It is therefore important that the scope of conditions in the text can apply to early-stage research, such as open sharing of research inputs, processes, and outputs, in addition to downstream manufacturing and licensing, which are already mentioned in the draft.

In addition to funding conditions, the CA+ should also include provisions to trigger immediate sharing of relevant IP when a PHEIC is declared, or following another agreed trigger, through the use of TRIPS flexibilities and other legal mechanisms, as referenced in Article 7.

DNDi suggests that the specific provision within Article 9 (e) is further clarified to reflect the end-to-end approach that is needed. In addition, references in other sections of the draft which seek to encourage recipients of public funding to take certain actions should be linked to specific conditions on public funding, including those in Article 7 (access to technology), Article 8 (regulatory), and the transparency elements in Article 9 (referenced below). This could be facilitated either by directly referencing 'via conditions in funding agreements' next to relevant obligations in these articles, and/or creating one area where the conditionalities are clarified and expanded as suggested below.

Article 9. 2 (e) could be expanded and become a new provision 9.2 bis with an expanded 9.2 chapeaux:

Article 9.2 bis: With a view to promoting greater sharing of knowledge, transparency, [ADD efficiency of R&D, and equitable access to health tools], each Party, when providing public funding for research and development for pandemic prevention, preparedness, response and recovery of health systems, shall, [ADD include binding terms and conditions on recipients of publicly funded research and development, which include:

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a) public dissemination and transparency of research **inputs** (including specimens, samples, compound libraires, and datasets with appropriate data protections), **processes** (including protocols, clinical trial design, and R&D costs), and **outputs** (including clinical trial results, open access publications, and data sharing);
b) affordable pricing of end products, including on a no-profit/no-loss basis upon PHEIC determination;
c) granting of non-exclusive licenses, including provisions for data sharing, technology transfer, and waiving or managing royalties as appropriate, to enable development, manufacturing, and distribution, especially in developing countries;
d) adherence to allocation frameworks as determined by WHO when PHEIC is declared; and
e) retention of rights by the funder, through ownership or licensing of research results, for use, licensing, or assignment, as necessary, to ensure affordable, equitable, and timely access.

Additional areas in the draft where reference should be made to conditions in funding agreements:

- Article 10 on Access and Benefit Sharing: to the extent that public funding is involved, conditionalities should be recognized in Article 10 as it is further developed. Additionally, linking benefits solely to access to end products fails to acknowledge the benefits of sharing other outcomes of research, including inputs, processes, and outputs, as well as IP, data, and know-how – all of which are critical to the efficient and equitable discovery and development of health tools.
- Article 9.10 (c) on transparent and rapid reporting of clinical research and clinical trial results
- Article 7 3 (c) on pro-access licensing terms

Provisions 9.2 (a), (c), (d) (which are unrelated to conditions) should remain and be expanded to include scientific cooperation across all countries

9.2. Parties should

(a) Promote the free, public dissemination of the results of publicly and government-funded research for the development of pandemic-related products
(b) Ensure that promotors of research for pandemic-related products assume an appropriate level of the associate risk;
(c) Promote and incentivize technology co-creation and joint venture initiatives, [ADD focusing on scientific cooperation to harness expertise across high-, middle-, and low-income countries, encouraging collaboration among research centres]

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4. Add provision for effective priority-setting processes

There is currently no reference to research priority-setting processes. The WHO CA+ should include measures to identify R&D needs and gaps, establish clear priorities through a transparent and inclusive process, and coordinate efforts to enhance collaboration and reduce duplication. COVID-19 highlighted that coordination challenges exist across the R&D ecosystem. The right framework is needed to bring stakeholders together and provide better coordination and alignment of national, regional, and international priorities. The CA+ should ensure that WHO is sufficiently empowered to play a strong normative role in helping define a priority research agenda and in coordinating research, building on the R&D Blueprint, to speed innovation and avoid duplication and fragmentation of data.

DNDi suggest the addition of a provision under Article 9 to include:

[ADD 4. Parties shall promote international cooperation in effective and transparent research priority-setting processes to develop effective and appropriate health tools that meet the needs of all people, with specific consideration given to people in vulnerable situations and to historically neglected communities, with a central role for WHO.]

5. Add provision for R&D financing obligations

There are currently no obligations linked explicitly to R&D financing. The WHO CA+ must include commitments for sustainable and predictable financing of end-to-end R&D that support open, collaborative approaches to discovery and development, with clear priority given to areas most likely to be neglected by the market.

Financing must avoid a narrowly defined focus only concerned with 'security threats' in high-income countries and break the cycle of panic and neglect for pandemics in which there is a surge of attention and investment during a crisis followed by years (or decades) of inaction when a threat is perceived to have subsided, in certain regions or globally, and innovation and manufacturing capacity is left idle. Financing must not only support R&D from 'bench to bedside' and ensure that unmet needs are prioritized, but ensure that there are adequate resources dedicated to developing and advancing medical technologies through the entire R&D pipeline, including mechanisms for rapid mobilization of public investments which are at risk.

DNDi suggest the addition of a provision under Article 9 to include:

[ADD 5. Parties shall contribute to sustainable, predictable international financing of R&D linked to public health priorities, both during and between pandemics].

Article 19 1 and 2 should make explicit reference to R&D financing.

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Recommendations for Article 9.10: clinical research ecosystems

6. Ensure measures to support regional clinical research ecosystems for preparedness and response by supporting new and existing clinical trial networks and infrastructure, especially those based in and led by low- and middle-income countries

We support the reference to developing strong and resilient national, regional, and international clinical research ecosystems and would encourage the scope to include not only pandemic response but also other existing health priorities to ensure sustainability and retain skills. Just as the response to COVID-19 depended on years of investment in clinical trial networks for other health threats, moving forward, it will be important to establish clinical trial infrastructure and platforms that can be flexible, autonomous, and able to respond promptly and effectively to emerging outbreaks – and in non-pandemic times, be capable of supporting efforts to tackle ongoing health priorities, for example neglected tropical diseases. Additionally, while efforts must be made to support existing infrastructure, it may be necessary to create new mechanisms.

Amend 9. 10 (a) to read: Fostering and coordinating clinical research and clinical trials, including, as appropriate though [ADD new and] existing coordination mechanisms [ADD , especially those based in and led by low- and middle-income countries];

7. Ensure that measures to strengthen clinical research ecosystems include a broad diversity of populations (Article 9)

Support for inclusive clinical trials is needed to improve equity and understanding of health outcomes within specific populations. There should be an explicit reference to the inclusion of underserved populations in all their diversity, including children and people who are pregnant or of child-bearing age. Disaggregating clinical trial result data is another important aspect and should remain as Article 9 10 (d).

8. Include measures to support regulatory authorities and ethics committees for clinical trial processes and oversight (Article 9)

Support for coordination and cooperation mechanisms for regulatory authorities and ethics committees is important in order to expedite and streamline clinical trial approval and review processes.

Add a new point to 9. 10 [ADD (e) supporting the coordination and cooperation of regional and national regulatory authorities and ethics committee for clinical trial approval processes and oversight.]

9. Obligations for the transparent and rapid reporting of clinical research and trial results should be strengthened (Article 9)

Transparency and timely publication of clinical trial protocols and results (both positive and negative) is critical for the harmonization of protocols/comparisons and coordination of treatment guidelines, as is the publication of cost of clinical trials, particularly when public funds are involved. Transparency can be enhanced through requirements to include this information in publicly available registers, such as ClinicalTrials.gov (NIH) and the Pan-African clinical trial registry, and can be obligated via conditions in funding agreements.

Amend Article 9 10 (C): [DEL supporting] [ADD ensuring] transparent and rapid reporting of clinical research and clinical trial results [ADD in publicly available registers and protocols, as well as publication of clinical trial costs, particularly when public funding is involved], to ensure evidence is available in a timely manner to inform national, regional and international decision-making, [ADD including via terms and conditions in funding agreements];

10. Include measures to ensure access to comparator and generic medical countermeasures for clinical trials (Article 9)

COVID-19 has highlighted barriers faced by generics and biosimilars companies in accessing originator products for reference products needed to conduct the necessary bioequivalence studies for regulatory approval, resulting in unnecessary delays and costs. Originator companies have also declined to provide access to relevant drugs for research purposes, for example for use in combination studies in low- and middle-income countries. Critically important public health research questions must be answered quickly during a pandemic, especially to determine optimal use of drugs, diagnostics, and vaccines in resource-limited settings. Therefore, the WHO CA+ should encourage access to comparator drugs, tests, vaccines, or assays needed for clinical trials in order to develop or compare technologies.

Add point to Article 9 10: [ADD 10 (f) encouraging access to comparator drugs, tests, vaccines, or assays needed for clinical trials to allow for rapid development or comparison of technologies]

Recommendations for Article 8: regulatory strengthening

11. Include obligations to ensure wide and rapid registration of health products, including where clinical trials have been conducted (Article 8)

Rapid registration should be obligated through multiple regulatory pathways to accelerate availably of health tools. Additionally, clinical trials are not the product of one party, organization, or company but of a collaboration, including strong reliance on the national systems in which they are conducted. It is therefore important that all those that contribute to the process have access to the end product. This includes the possibility of a requirement that technology is registered and available for the country and community where the clinical trials have been run, beyond clinical trial participants. Such approaches can also be obligated within the conditions of funding agreements.

Add a new point to 8 [ADD (4) Ensure and promote, including via conditions in funding agreements, wide and rapid registration of health tools, including where clinical trials have been conducted]

General recommendations

15) The INB process should provide the overarching framework for PPR and health emergencies

The WHO CA+ will be emerging in a broader context and as part of a major reshaping of the global pandemic preparedness and response architecture. To ensure policy alignment and coherence between the various other critical initiatives and mechanisms that are emerging, it is important that the WHO CA+ both provide an overarching framework for, and 'connect the dots' between, these various

initiatives. This includes discussions occurring in the G20 and other fora on a proposed platform for the development and equitable access to medical countermeasures. The implications of this proposal and its potential effects, including on Article 15 on coordination and collaboration, and the relevant R&D Articles 7, 8, 9 and 10, should be discussed as part of the INB process.

12. **WHO CA+ should consistently address the needs and vulnerabilities of individuals and groups at higher risk and in vulnerable situations throughout the text**

DNDi welcomes the recognition under Article 4(13), 14 2 (a)(ii) and 15 1 (c) of the rights of individuals and groups at higher risk and in vulnerable situations. However, addressing vulnerabilities specific to those groups must also be integrated throughout the text, including in the sections relating to R&D in Articles 7, 8, and 9. For example, children, and especially neonates, are at particular risk of morbidity and mortality due to drug-resistant infections, with 140,000 newborn deaths directly attributable to antimicrobial resistance in 2019.