

Terms of Reference for the Technical Advisory Group on dosing of TB medicines for adults and children

Tuberculosis (TB) remains one of the world's deadliest infectious killers and is a major cause of ill health and suffering for millions. Until the coronavirus disease (COVID-19) pandemic, TB has ranked as the top cause of death due to a single infectious agent. This situation is again reversing, following the fall in COVID-19-related deaths. In 2021, an estimated 10.6 million people fell ill with TB, (including 1.15 million children) and 1.6 million people died of TB. Globally, the success rate for people treated for TB in 2020 was 86%. However, without treatment, the death rate from TB disease is high (about 50%). The burden of drug-resistant forms of TB is estimated to have increased between 2020 and 2021, with an estimated 450 000 new cases of rifampicin-resistant TB (RR-TB) in 2021. Stopping TB infection from progressing to disease by TB preventive treatment (TPT) is a critical and effective intervention to reduce TB incidence to the levels envisaged by the End TB Strategy.

Recent years have seen significant advances in terms of the scientific evidence generated on shorter regimens for both TB treatment and TB prevention. Results from several studies have informed WHO recommendations on regimens for drug-susceptible TB with a duration as short as 4 months and for regimens for MDR/RR-TB with a duration as short as 6 months, as well as TPT regimens with a duration down to 1 month. Access to shorter, simpler regimens is a key aspect to improve people-centred TB care.

To keep pace with these developments, the WHO Global Tuberculosis Programme develops evidence-informed policy as new evidence becomes available. As many of the new policy recommendations are at the cutting edge of the science, important practical questions remain related to the implementation of treatment of TB infection and disease, which are beyond the scope of the WHO guideline development process, and which require additional evidence and critical evaluation from technical experts.

In parallel to new evidence being generated that informs WHO recommendations, several studies have been conducted or are ongoing to optimize TB medicine dosing strategies among children and adults, given available formulations of TB medicines and considering particularly vulnerable populations, TB-HIV co-infection and severe forms of extra-pulmonary TB.

In this context, a Technical Advisory Group on dosing of TB medicines for adults and children, composed of experts on pharmacokinetics/pharmacodynamics, pharmacometricians, researchers, clinicians, including paediatricians, with the mandate and principles set out below, is being convened to assist WHO to address dosing issues related to TB medicines for all indications, aligned to WHO recommendations.

The Advisory Group (the "AG") will act as an advisory body to WHO in this field.

I. Functions

In its capacity as an advisory body to WHO, the AG shall have the following functions:

1. *To provide an independent evaluation and advice to WHO on scientific and technical aspects of dosing of anti-tuberculosis medicines for children and adults with all forms of TB, aligned to WHO recommendations and based on the latest available scientific evidence with the aim to optimize the dosing of TB medicines and the operational guidance on their use by country programmes;*
2. *To advise WHO on the new developments in the dosing and drug delivery approaches of medicines used in TB care.*

II. Composition

1. The AG shall have up to 20 members¹, who shall serve in their personal capacities to represent the broad range of disciplines relevant to dosing of TB medicines in adults and children. In the selection of the AG members, consideration shall be given to attaining an adequate distribution of technical expertise, geographical representation and gender balance.
2. Members of the AG, including the Chairperson, shall be selected and appointed by WHO following an open call for experts. The Chairperson's functions include the following:
 - to chair the meetings of the AG;
 - to liaise with the WHO Secretariat between meetings.

In appointing a Chairperson, consideration shall be given to gender and geographical representation.

3. Members of the AG shall be appointed to serve for a period of 3 years and shall be eligible for reappointment. A Chairperson is eligible for reappointment as a member of the AG, but is only permitted to serve as Chairperson for one term. Their appointment and/or designation as Chairperson may be terminated at any time by WHO if WHO's interest so requires or, as otherwise specified in these terms of reference or letters of appointment. Where a member's appointment is terminated, WHO may decide to appoint a replacement member.
4. AG members must respect the impartiality and independence required of WHO. In performing their work, members may not seek or accept instructions from any Government or from any authority external to the Organization. They must be free of any real, potential

¹ Members serve as full participants and partake in the deliberations and the adoption of the recommendations of the meeting in which they are involved.

or apparent conflicts of interest. To this end, proposed members/members shall be required to complete a declaration of interests form and their appointment, or continuation of their appointment, shall be subject to the evaluation of completed forms by the WHO Secretariat, determining that their participation would not give rise to a real, potential or apparent conflict of interest.

5. Following a determination that a proposed member's participation in the AG would not give rise to a real, potential or apparent conflict of interest, the proposed member will be sent a letter inviting them to be a member of the AG. Their appointment to the AG is subject to WHO receiving the countersigned invitation letter and letter of agreement. Notwithstanding the requirement to complete the WHO declaration of interest form, AG members have an ongoing obligation to inform the WHO of any interests real or perceived that may give rise to a real, potential or apparent conflict of interest.
6. As contemplated in paragraph II.4 above, WHO may, from time to time, request AG members to complete a new declaration of interest form. This may be before a AG meeting or any other AG-related activity or engagement, as decided by WHO. Where WHO has made such a request, the AG member's participation in the AG activity or engagement is subject to a determination that their participation would not give rise to a real, potential or apparent conflict of interest.
7. Where a AG member is invited by WHO to travel to an in-person AG meeting, WHO shall, subject to any conflict of interest determination as set out in paragraph II.6 above, issue a letter of appointment as a temporary adviser and accompanying memorandum of agreement (together 'Temporary Adviser Letter'). WHO shall not authorize travel by an AG member, until it receives a countersigned Temporary Adviser Letter.
8. AG members do not receive any remuneration from the Organization for any work related to the AG. However, when attending in-person meetings at the invitation of WHO, their travel cost and per diem shall be covered by WHO in accordance with the applicable WHO rules and policies.

III. Operation

1. The AG shall normally meet at least once each year. However, WHO may convene additional meetings. AG meetings may be held in person (at WHO headquarters in Geneva or another location, as determined by WHO) or virtually, via video or teleconference.

AG meetings may be held in open and/or closed session, as decided by the Chairperson in consultation with WHO.

- (a) Open sessions: Open sessions shall be convened for the sole purpose of the exchange of non-confidential information and views, and may be attended by Observers (as defined in paragraph III.3 below).

(b) Closed sessions: The sessions dealing with the formulation of recommendations and/or advice to WHO shall be restricted to the members of the AG and essential WHO Secretariat staff.

2. The quorum for AG meetings shall be two thirds of the members.
3. WHO may, at its sole discretion, invite external individuals from time to time to attend the open sessions of an advisory group, or parts thereof, as “observers”. Observers may be invited either in their personal capacity, or as representatives from a governmental institution / intergovernmental organization, or from a non-State actor. WHO will request observers invited in their personal capacity to complete a confidentiality undertaking and a declaration of interests form prior to attending a session of the advisory group. Invitations to observers attending as representatives from non-State actors will be subject to WHO internal due diligence and risk assessment including conflict of interest considerations in accordance with the Framework for engagement with non-State actors (FENSA). Observers invited as representatives may also be requested to complete a confidentiality undertaking. Observers shall normally attend meetings of the AG at their own expense and be responsible for making all arrangements in that regard.

At the invitation of the Chairperson, observers may be asked to present their personal views and/or the policies of their organization. Observers will not participate in the process of adopting recommendations of the AG.

4. The AG may decide to establish smaller working groups (sub-groups of the AG) to work on specific issues. Their deliberations shall take place via teleconference or video-conference. For these sub-groups, no quorum requirement will apply; the outcome of their deliberations will be submitted to the AG for review at one of its meetings.
5. AG members are expected to attend meetings. If a member misses two consecutive meetings, WHO may end his/her appointment as a member of the AG.
6. A yearly report shall be submitted by the AG to WHO (the Assistant Director-General of the responsible Cluster). All recommendations from the AG are advisory to WHO, who retains full control over any subsequent decisions or actions regarding any proposals, policy issues or other matters considered by the AG.
7. The AG shall normally make recommendations by consensus. If, in exceptional circumstances, a consensus on a particular issue cannot be reached, minority opinions will be reflected in the meeting report.
8. Active participation is expected from all AG members, including in working groups, teleconferences, and interaction over email. AG members may, in advance of AG meetings, be requested to review meeting materials and to provide their views for consideration by the AG.
9. WHO shall determine the modes of communication by the AG, including between WHO and the AG members, and the AG members among themselves.

10. AG members shall not speak on behalf of, or represent, the AG or WHO to any third party.

IV. **Secretariat**

WHO shall provide the secretariat for the AG, including necessary scientific, technical, administrative and other support. In this regard, the WHO Secretariat shall provide the members in advance of each meeting with the agenda, working documents and discussion papers. Distribution of the aforesaid documents to Observers will be determined by the WHO Secretariat. The meeting agenda shall include details such as: whether a meeting, or part thereof, is closed or open; and whether Observers are permitted to attend.

V. **Information and documentation**

1. Information and documentation to which members may gain access in performing AG related activities shall be considered as confidential and proprietary to WHO and/or parties collaborating with WHO. In addition, by counter signing the letter of appointment and the accompanying terms and conditions referred to in section II(5) above, AG members undertake to abide by the confidentiality obligations contained therein and also confirm that any and all rights in the work performed by them in connection with, or as a result of their AG-related activities shall be exclusively vested in WHO.
2. AG members and Observers shall not quote from, circulate or use AG documents for any purpose other than in a manner consistent with their responsibilities under these Terms of Reference.
3. WHO retains full control over the publication of the reports of the AG, including deciding whether or not to publish them.