

Terms of Reference for the Technical Advisory Group on Snake Antivenom Immunoglobulin Listing (TAG-SAIL)

The World Health Organization (WHO), acting through its Regulation and Prequalification Department has issued a call for applications to licensed manufacturers of snake antivenom immunoglobulin products who wish to have those products evaluated for potential procurement recommendation listing by WHO. The call for applications applies to antivenoms manufactured for the treatment of the following WHO category 1 medically important snake species:

- Common krait (*Bungarus caeruleus*)
- Russell's viper (*Daboia russelii*)
- Saw-scaled viper (*Echis carinatus*)
- Indian cobra (*Naja naja*)

Products for the treatment of envenoming by these species are typically marketed in Pakistan, India, Nepal, Bangladesh, Bhutan, and Sri Lanka.

In 2018 the World Health Assembly adopted resolution 71.5 (2018: *Addressing the burden of snakebite envenoming*) which calls on WHO to ensure the quality and safety of snake antivenoms. WHO has developed a risk-benefit assessment procedure for snake antivenoms, to assist interested WHO Member States, United Nations' procurement agencies, international organizations and other stakeholders in determining the acceptability of using specific snake antivenom products, based on an evaluation of an essential set of available quality, safety, efficacy, and performance data. Furthermore, it provides manufacturers with independent product analysis, evaluation of Good Manufacturing Practices (GMP) and potential product recommendation. The risk-benefit assessment process is aimed at improving the availability of safe, effective antivenom immunoglobulin products to all who need them.

As part of this procedure, the WHO Secretariat will require advice from an independent advisory group known as the Technical Advisory Group on Snake Antivenom Immunoglobulin Listing (TAG-SAIL) on whether or not these risk-benefit assessed antivenoms can be recommended for use.

The aforementioned 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 undertake a desktop review and risk-benefit assessment of the product dossiers submitted to the WHO Secretariat by respective manufacturers and prepare product dossier reports for WHO indicating specific deficiencies, data gaps and other areas of concern.
2. To subsequently consider the results of independent laboratory analysis of antivenom products, and the outcomes of Good Manufacturing Practice (GMP) inspections.
3. For each snake antivenom product submitted for WHO assessment, to conduct a risk-benefit assessment of such product's potential use for the treatment of the abovementioned WHO category 1 medically important snake species.

4. Based on the findings of the product dossier reviews, laboratory analyses and GMP inspections, to make recommendations to WHO on whether the assessed antivenoms should be listed as recommended product under the SAIL procedure, and under what conditions.
5. To advise on formulating conditions for the listing should the decision be positive. Conditions will include detailed post-listing commitments from the manufacturer.

II. Composition

1. The AG shall have up to 12 members, who shall serve in their personal capacities to represent the broad range of disciplines relevant to risk-benefit assessment of snake antivenom immunoglobulins. In this respect, the AG will include members with expertise in the fields of:
 - Regulation of biological products such as vaccines or antivenoms;
 - Veterinary medicine related to animal use in production of biological products;
 - Manufacturing or quality control technologies related to biological products;
 - Good Manufacturing Practice (GMP) for biological products;
 - Clinical management of snakebite envenoming in Pakistan, India, Nepal, Bangladesh, Bhutan, or Sri Lanka; and
 - Viral inactivation of equine or other viruses in biological products.

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 meeting 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 two 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. A member's 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. AG members must be free of any real, potential, 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 an 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 an 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 twice 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 internal due diligence and conflict of interest considerations in accordance with 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 decisions and 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. Reports of each meeting with the recommendation of the snake antivenom product under discussion shall be submitted by the AG to WHO (to the attention of 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 documentation 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.