Ad hoc working group

for

Diphtheria Antitoxin (DAT)

Terms of Reference

23 November 2017
Introduction
Given the limited supply of equine Diphtheria Antitoxin (DAT), the mandate of the Ad Hoc Working Group is to propose options to ensure rapid provision, therefore the WG should review and explore mechanisms and strategies for production, supply and stockpiling.

Objectives
The specific objective is to ensure that any population experiencing cases or an outbreak of diphtheria has rapid and easy access to equine DAT. The ad hoc working group will develop short-term and a long-term strategies for countries willing to maintain national stockpiles on their own and a global/ regional stockpile for countries that have no means to maintain and finance a stock.

Specifically the Working Group will be asked to work on the following elements:

Short Term

- Collect information on all manufacturers currently or in the near future capable of producing equine DAT
- Collect, summarize and assess data on equine DAT products produced by each manufacturer (including potency, GMP, quality control, exclusion of selected adventitious agents and veterinary inspection certificate)
- Assess available equine DAT supply, production capacity and production lead-times including regulatory approvals
- Collect requirements for authorisation and use of equine DAT in each WHO region. (emergency use authorization, compassionate use, Investigational New Drug applications, etc).
- Develop procurement strategies for the short term (advance procurement, Long term Agreements, firm commitment) to incentivise production
- Estimate equine DAT demand, in consultation with partners that already expressed interest in procuring and stockpiling (CDC, EC (through ECDC), UNICEF, MSF, WHO)
- Develop minimum criteria for selection of at least two equine DAT suppliers to ensure availability
- Develop procurement mechanisms to enable individual countries, joint procurement for a group of countries (e.g. European Union and PAHO), other entities (MSF) in addition to procurement by UNICEF
- Coordinate the demand and procurement among the agencies to avoid competitions and communicate to the suppliers

Mid-long term

- Propose options for development and maintenance of equine DAT stockpiles (e.g. by country, by region and central for countries which will not have stockpiles)
• Propose a mechanism for emergency use of equine DAT stockpile: members, necessary information to be provided to have access, criteria for release, secretariat, procurement, etc.
• Explore pros and cons of having centralized versus regional equine DAT stockpiles, possible locations
• Propose solutions to harmonize product specifications and QC of equine DAT
• Explore prequalification of equine DAT including testing and standardization
• Explore technology transfer of equine DAT production
• Explore standardized pre-clinical and clinical testing, authorisation and use of available and new monoclonal antibodies instead of equine DAT for treatment (MassBiologics, USA and possibly Technische Universität Braunschweig, Germany)

Ad hoc WG Composition and overview of available equine DAT stockpiles
The organizations that have already expressed interest to procure treatment for diphtheria are:
- Center for Disease Prevention and Control in the USA (US CDC). The Center is holding a smaller stockpile of outdated equine DAT that could be used in occurrence of individual cases or an outbreak under an IND protocol. Potency testing conducted regularly shows residual neutralizing activity.
- European Commission (EC) under the Joint Procurement Agreement (European Centre for Disease Prevention and Control (ECDC) is providing technical support to the EC). In the European Union countries taking part in the Joint procurement mechanism are foreseen to hold individual stockpiles in each country. Many but not all EU/EEA countries have a smaller stockpile of outdated equine DAT. Potency testing conducted regularly shows residual neutralizing activity.
- World Health Organization, is procuring during emergency outbreaks upon request of countries
- UNICEF SD: currently procuring equine DAT on a routine basis on behalf of countries
- MSF: procures as response to emergency outbreaks and provide case management
- Regulatory agencies, FDA, EMA and WHO, will provide advice and help to harmonize criteria for emergency approvals, regulatory preparedness for outbreak response, generic protocols for compassionate use/expanded access, EUAL for equine DAT and monoclonal antibodies.
- For short-term selection of at least two suppliers: Rapid quality assessment criteria of product and production site inspections (WHO, Regulators)
- Laboratory expertise to assess DAT potency and possibly exclude adventitious viruses in line with European and other requirements (NIBSC, PEI)
- Procurement and stockpile management for countries in need (WHO, CDC, MSF, UNICEF)

### Proposed members

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<tr>
<th>Organization</th>
<th>Member</th>
<th>Contact details</th>
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| UNICEF SD             | Heather Deenan        | Tel: +45 4533 5890  
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|                       | Mark Muscat           |                                                                      |
| European Commission (EC) | Wolfgang Phillip   | Email: Wolfgang.PHILIPP@ec.europa.eu                                    |
| ECDC                  | Aisha Sauer           | Email: Aisha.SAUER@ec.europa.eu                                         |
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| US FDA                | Dorothy Scott, M.D.,  | Tel: 1-240-402-8236  
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|                       | Michael Kennedy       | Tel: 1-240-402-9332                                                     |
Membership in the group should be confirmed by respective agencies, based on availability/involve ment and technical expertise.

Lack of conflict of interest: members must not have any involvement with the vaccine industry e.g. perform consultancies for and/or receive funding from such manufacturers.

**Responsibilities**

WHO will act as secretariat and will convene the TCs or face-to-face meetings.

The Members of the ad hoc working group should be available for telephone conferences, consultation and eventually for meetings in person.

Since most of the tasks for the short term are collection of information, Members of the WG may also be requested to perform some of the activities and to share the available information with the rest of the Working group and the WHO secretariat.

**Modus Operandi**

When needed or upon request of any of the Members, the secretariat will organize teleconferences. The telephone conferences will be organized at a time of the day to allow PAHO and WPRO offices to participate.

Discussion will also be carried out by email.

WHO secretariat will chair the first TC, then it can rotate among the Members.

WHO will also organize in person meetings when members consider necessary.

Decisions and recommendations will be made by consensus.

**Confidentiality**

Most likely the information obtained by the manufacturers will be confidential and should not be shared beyond the Working group. Exceptions to this may be considered at the time of procurement. Members of the group and the secretariat must commit to respect the confidentiality of data.

The secretariat will limit information sharing to the Members of the group.

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<tr>
<th>Organization</th>
<th>Name</th>
<th>Phone</th>
<th>Email</th>
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<tbody>
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Communication
Outcomes of the discussions and recommendations will be published on the WHO website. Availability of equine DAT could be available in WHO and UNICEF SD dashboards similar to the current vaccine stockpiles for Meningitis, Cholera and Yellow Fever vaccines.