

DCVMN 3Rs Project Diphtheria-Tetanus Single Dilution Assay for Potency Calculation Implementation Plans.

Rationale and Objectives

The single dilution assay for the potency calculation of Diphtheria-Tetanus containing vaccines reduce the number of animals required for both the in vivo challenge and the serological potency assay.

The single dilution is performed when the potency of the test vaccine consistently and significantly exceeds minimum requirements (i.e., the potency of the test vaccine is significantly greater than the minimum requirement per human dose for the product under test) and when parallelism between test and reference vaccine has been demonstrated over time.

An amendment to the diphtheria and tetanus sections of wP containing vaccines concerning single dilution and in vitro potency assays was adopted by the Expert Committee on Biological Standardization in 2004 (c.f. *Requirements for Diphtheria, tetanus, pertussis and combined vaccines. In: WHO Expert Committee on Biological Standardization. Fortieth report. Geneva, World Health Organization, 1990, Annex 2 - WHO Technical Report Series, No. 800*) and the single dilution is included into the Tetanus and Diphtheria TRS 980 and into the WHO Manual for Quality Control of Diphtheria, Tetanus and Pertussis Vaccines (IVB 11.11, 2013).

The objectives of the projects are:

- A) Identify DCVMN members interested in implementing the single dilution assay in both the in vivo challenge and in the serological potency assay.
- B) Support the members participating to the project to create implementation plans (one per each company) of the single dilution assay. Members will receive dedicated support from external experts depending on whether they will implement it for the in vivo challenge or the serological assay.
- C) Create a communication channel between members and external experts on the topic, allowing all the parties to safely communicate respecting each other's confidentiality.

The project does not include support to members interested to transition from the in vivo challenge to the serological assay. If a minimum of 5 companies are interested to the transition from the in vivo to the serological assay, DCVMN will consider organizing a separate project and seek experts and funds.

The participation to the project does not make the implementation of the Single Dilution Plans mandatory. However, if further technical support to move into the implementation phase is requested by a minimum of 5 laboratories, a second project may be considered and additional funds sought. Similarly, if a minimum of 5 laboratories request for face to face training, DCVMN could facilitate that and seek for funds.

Project Description

The project is managed by DCVMN Secretariat that coordinates the work of the external experts and their interaction with the company members participating to the project.

Initiation and planning

DCVMN will set up agreements with external experts or a group of experts that will provide the scientific and technical guidance and documentation to allow participating members to create their own Single Dilution Implementation plans.

DCVMN members that have successfully implemented the Single Dilution could join DCVMN and the external experts in preparing the opening workshop and any ad hoc workshops that will be organized

within the timeframe of the project. The DCVMN members joining as “industry experts” won’t participate to the review of the Single Dilution Implementation plans.

A questionnaire will be sent to all the DCVMN members interested in participating to gather preliminary information that will help the organization of the opening workshop and the subsequent work (i.e., to which assay the Single Dilution should be implemented: in vivo challenge or serological assay; type of product in scope: D, T, or combinations; etc.). Based on the questionnaire responses, DCVMN and the external experts (and any DCVMN members “industry experts”) will organize the opening workshop.

Implementation

The opening workshop will be held to provide with scientific, technical and regulatory guidance on the implementation of the Single Dilution Assay and kick-start the project.

Based on the result of the questionnaire two working groups may be established – one for members aiming to implement the Single Dilution for the in vivo challenge, one for the ones aiming to implement the Single Dilution for the serological assay). The two working groups will participate to at least one technical workshop where further guidance and technical support is going to be provided by the external experts.

DCVMN in agreement with the laboratories might invite local regulatory authorities’ representatives to the opening technical workshop, and/or to the next ones, as a way to facilitate further independent outreach and dialogue between them and the companies. If their participation is agreed, regulatory authorities’ representatives won’t get access to any confidential materials, only to what is going to be shared during the technical workshop.

Each company will work independently on its Single Dilution Implementation plan. DCVMN approved external experts, will provide support to the companies in the instance technical difficulties arise during the drafting of individual implementation plans. If one or more topics emerge as critical, a dedicated workshop can be organized.

The Single Dilution Implementation plans will be submitted to DCVMN that will make sure to anonymize them and distributed within the external experts for their review.

Closure

The DCVMN external experts will review the proposed plans twice and provide a generalized feedback session which can be attended by all DCVMN members.

Project Timelines

	M0	M1	M2	M3	M4	M5	M6
Members Engagement and questionnaire							
External Experts Agreements							
Opening workshop							
Working groups (members & experts)							
Workshops							
Members working on their plans							
Review of the plans							
Feedback to members							

Participants profile

Quality Control and Regulatory Affairs experts.