DCVMN, October 2022

CENTER FOR VACCINE INNOVATION & ACCESS

Innovation in Vaccine Technology –

A case study with polio vaccines

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A paradigm shift..

~ 10yrs





~ 100 days



Initial Costs	
Training	\$600
Insurance	\$1,000-6,000
Admin	\$4,000-\$7,500
Pilot	\$4,000-\$11,000
Compliance'	\$20,000
Equipment	\$3,000-\$30,000
Total	\$32,600-\$75,100

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2022 Only two endemic countries

Live Poliovirus Containment



Necessity- the mother of innovation

- Manufacturing Process for all three types of polioviruses
 - Sabin S19 virus backbone for expression of capsid proteins
 - Non-infectious VLP as vaccine candidates
- Alternative testing platforms for vaccine release
 - Release testing
- Regulatory Endorsement
 - NRAs
 - ≻ WHO

Alternate Release Testing Platform

Next Generation Sequencing (NGS)- An alternative to animal based neurovirulence testing (NVT) of polio vaccines

Current State

- Animal Safety Testing for neurovirulence performed routinely
- Largest number of animals used in NVT for any vaccine safety testing that is animals based. Very expensive (> \$300K)
- > NVT is performed in monkeys (M-NVT) or polio-virus receptor transgenic mice (Tgm-NVT).
- 72 monkeys or 80 Tg mice for QC release of one lot. Monkeys use restricted in some countries, and only one supplier of Tgm mice.
- Need highly trained expertise in intra-spinal inoculations. Very few labs can perform NVT (currently with GAP-III containment)
- In mid-1990s attempt to partially replace animal testing, with an alternative *in vitro* assay that directly measures the amount of revertants by mutant analysis by PCR and restriction enzyme cleavage (MAPREC) was introduced as an *in vitro* lot release test.
- MAPREC can monitor only a limited number of genomic loci known to contain the markers of attenuation and miss mutations at other sites. For this reason, animal testing is still required during vaccine production.
- > Replacement of animal testing with *in vitro* molecular surrogate assays is highly desirable.

• Polio NGS - Key Activities

- Test Sabin type 1, 2, and 3 vaccine materials by next generation sequencing (NGS) to establish whole genome profiles and determine consistency in different production runs. Comparison of NGS results with those from standard animal neurovirulence test (NVT).
- > Development of bio-informatics software tool for NGS analysis
- > Align with WHO ECBS for replacing animal NVT with in vitro NGS whole genome analysis test.
- Plan and execute collaborative study to assess utility of NGS method for the whole genome profile of Sabin polioviruses types 1, 2, and 3.
- Conduct workshop to discuss:
 - Results of NGS collaborative studies for Sabin types 1, 2, and 3.
 - > Next steps towards validation and implementation of assay.
 - > Development of pass-fail decision criteria.
- Submit collaborative study report to WHO ECBS on endorsement for replacing animal NVT with in vitro NGS whole genome analysis test.
- > Revise WHO TRS following WHO ECBS endorsement.

NGS collaborative study report for oral polio vaccine type 1 and 2



WHO/BS/2022.xxxx ENGLISH ONLY

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION Geneva, 24 to 28 October 2022

Report on the WHO collaborative study to investigate the utility of next generation sequencing (NGS) of virus stocks used in the manufacture of Type 1 and 2 Poliovirus vaccine (Oral)

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NOTE:

This document has been prepared for the purpose of inviting comments and suggestions on the proposals contained therein, which will then be considered by the Expert Committee on Biological Standardization (ECBS). Comments MUST be received by **23 September 2022** and should be addressed to the attention: World Health Organization, 1211 Geneva 27, Switzerland, attention: Technical Standards and Specifications (TSS). Comments may also be submitted electronically to the Responsible Officer: **Dr Ivana Knezevic** at email: knezevici@who.int.



Next steps

- ✓ Accumulate NGS data for OPV1 and OPV2 for 5'-UTR neurovirulent mutations
- Accumulate whole-genome NGS data for all three serotypes
- Development of an optimal bioinformatics pipeline
- Consensus on the PASS/FAIL acceptance criteria
- Develop reference materials for NGS
- Collaborative study
 - Commitment to participate in the study
 - Test a set of samples provided to all participants
 - Test consecutive batches of OPV to establish the range of variations
 - ECBS endorsement

Collaborative Partners







In Partnership with:

OPV & IPV Manufacturers (DCVMNs) & National Laboratories



BILL& MELINDA GATES foundation

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In loving memory of Dr. Suresh Jadhav



