Poster presentation abstract

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Replacing the Lethal Guinea Pig Challenge with an in vitro Potency Assay for Diphtheria

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The US Diphtheria potency test (USPHS) is used for release of multiple diphtheria toxoid containing combination vaccines produced by Sanofi Pasteur. In the USPHS test, serum from guinea pigs immunized with the vaccine is mixed with a lethal dose of diphtheria toxin and subsequently injected into naive guinea pigs, with a readout of survival/death. Potent vaccine products are expected to elicit neutralizing antibodies that protect animals from the lethal effect of diphtheria toxin, while negative control animals will not survive.

As part of the 3R initiative to reduce, refine, and replace the use of animals in testing, we developed an in vitro assay to replace the lethal challenge portion of the USPHS.

The Diphtheria Vero cell (DVC) assay was developed as a sensitive, semi-quantitative cell-based test that directly demonstrates the mechanism of action of the diphtheria component of the vaccine. It is an endpoint titre assay which measures the neutralization titre of serum from immunized guinea pigs thus negating the need for lethal challenge. The DVC assay is precise, robust and less variable than the in vivo lethal challenge in USPHS assay.

The assay aligns with the USPHS in terms of reportable value (Units/mL) to the US reference antiserum so that existing product specifications can be used. The DVC Assay is currently undergoing concordance testing using diphtheria vaccines manufactured in SP Toronto. When accepted, the use of the DVC assay will have a huge impact on reducing animal use in the USPHS compendial test with expected reduction of animal use by 22% per test plus the costs associated with the use of animals.

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Note: All animal use was carried out in accordance with all applicable animal care and use laws, regulations, and guidelines. The study was approved by Animal Care and Use Committee.