Potency testing for NTD vaccines: determining relative potency for the Na-GST-1 Hookworm Vaccine

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Abstract

Over the next decade, a new generation of vaccines will target the neglected tropical diseases (NTDs). The goal of most NTD vaccines will be to reduce the morbidity and decrease the chronic debilitating nature of these often lifelong infections—outcomes that are hard to measure in the traditional potency testing paradigm. The absence of measurable correlates of protection, lack of efficacious animal models for lethal infection, and a lack of clinical indications that do not include the induction of sterilizing immunity required to reconsider the traditional biochemical methods for determining vaccine potency. Having to these limitations, potency assay design for NTD vaccines will increasingly rely on a paradigm where potency testing is one among many tools to ensure that a manufacturing process yields a product of consistent quality.

Introduction

The 4-parameter standard reference curves were generated at multiple time points.

Standard Reference Serum

Standard Reference Serum was generated by vaccinating sixty Balb/c mice with NaGST-1 vaccine. The ED50 was obtained using the graphical interpolation methods described in European pharmacopeia. Here, the relative potency compare the relative potency of Na-GST-1 vaccine at time zero and month 12 post manufacture.

Methods

The Na-GST-1 vaccine was found to be 1.00, 2.49, 2.84, 2.35, 16.49 at 0, 3, 6, 9, and 12 months post manufacture respectively. The upper 95% fiducial limits of the relative potency is not less than 0.5.

Figure 4. Global Standard Reference Curve

Figure 5. Response Threshold (Global Standard Reference Curve)

Figure 6. ED50 using probit transformed percent responders

Table 2. ED50 and Relative Potency

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<thead>
<tr>
<th>ED50(µg)</th>
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Relative Potency

The specification submitted in our IND states, “The criterion for acceptance is that the upper fiducial limit of the estimated relative potency is not less than 0.5.”

Conclusion

The Na-GST-1 vaccine gained potency within the first three months of storage at 4°C and remain immunogenic 12 months post manufacture. We proposed that the gain in potency within the first three months coincides with the higher affinity binding of the Na-GST-1 to the Alhydrogel® that occurred during storage at 4°C.

References


Acknowledgments

The authors wish to acknowledge Bruce J. Meade and Jane Helmers for their inspiration, advice and guidance as they came to understand how to develop a potency assay for a neglected tropical disease vaccine. They would also like to thank David Cronin, Canida Wa Maria, Kathryn Jones and Bin Zhan for their support of this project. This project is supported by the Sabin Vaccine Institute through funding of the Bill and Melinda Gates Foundation. The authors have no other potential financial or material interests or relationships with any organization or entity with a financial interest or financial conflict with the subject matter or materials discussed in this paper from those disclosed.

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The Na-GST-1 vaccine shows increased potency at each of the tested time points compared to its potency at the time of manufacture.

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