Table 29: Potency Testing for Vaccine Development

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**SCOPE:**

At this table we will discuss on how to design and set up appropriate *in vitro* potency methods in support of vaccine development. Ideally, the *in vitro* potency methods should reflect the mode-of-action (MOA) of the vaccine, or, if possible, the correlate(s) of protection (COP). Such correlates are often unknown, which challenges method choice and design.

The scope of this table is limited to *in vitro* potency methods for prophylactic vaccines.

**QUESTIONS FOR DISCUSSION:**

1. How are MOA and/or COP typically defined and/or identified?

2. What are typical activities that are performed to link the *in vitro* potency method to the MOA or COP?

3. How to incorporate the information from non clinical (animal models) / clinical studies and immunogenicity assessments?

4. What challenges have you experienced in developing *in vitro* potency assays for your vaccine?

5. What types of in vitro assays have people used/ tried? Was this successful? Have these been approved by regulatory authorities?

6. How are specifications set for vaccine potency? Are results from the clinic taken into account for setting acceptance criteria?

7. Do people use relative potency for vaccines? How is the reference standard defined? What are the requirements/desires for precision and accuracy of potency methods?

8. How do companies balance the desire to acquire more information on a new molecular entity with the need to limit resource investment prior to POC? What do companies do at which phase of development regarding potency assays?

**NOTES:**

- In vitro potency assay development for Mechanism of Action (MOA) or Correlate of Protection (COP)
  - For many vaccines we don’t know the MOA or the COP
  - If MOA/COP known, feasibility of in vitro potency testing increases.
  - It’s a common goal to hope to remove in vivo assay for licensure and just run an in vitro assay. However it is likely that some type of in vivo testing will be required throughout clinical development to support the vaccine program.

- Viral vector vaccines expressing a recombinant protein
  - The virus has to get into the cells. Need an infectivity assay. Phase 1. Infectivity is the primary MOA.
The antigen needs to be expressed. Need an antigen expression assay. Phase 3. This must be quantitative, not just qualitative.

The antigen must develop an immune response. Need an immunogenicity assay.

You may not know the epitopes that correlate to protection, so an in vivo assay may be needed to confirm potency.

Suitable animal models are not always available.

These vectors may be a non replicating virus, many are. Note that yellow fever vaccine infects but is not pathogenic. It does stimulate protection against the pathogenic strains.

Is the sequence of the DNA insert sufficient to confirm the right antigen will be expressed? Likely not, as a lot needs to happen beyond that.

- A Definition of Potency
  - Look up the potency assay definition in the CFR.
  - What is going on and what has to happen for the vaccine to work.
  - Does a vaccine behave in a cell based in vitro assay the same way it will in an in vivo assay? You would need in vivo data to prove this.
  - Whether it’s in vivo or in vitro, it’s a measure of the ability of the product to achieve the desired effect.
  - It must demonstrate a dose response.
  - Note that the polysaccharide conjugate vaccines essentially measure the mass of the vaccine for “potency”. Physiochemical assessment is used to establish potency, as correlated to clinical efficacy

- Consistency Approach
  - You must demonstrate that your vaccine is consistent to the lots used in the clinical efficacy trials. Use characterization data for this along with release data.
  - You need to establish that every lot is comparable
  - Physiochemical data can be used to support the potency data to establish that a vaccine is comparable
  - Characterize your vaccine as best you can
  - For protein vaccines, test all the lots with in vitro and in vivo assays to demonstrate trends in both to evaluate if in vitro is sufficient
  - Potency assay has to be connected to the process. If you change the process, the potency assay may pick up a change that may or may not be “real”.

- Adjuvants
  - The impact of adjuvants (such as alum) cannot really be evaluated when using an in vitro assay (either antibody based or cell based)
  - An in vivo test will evaluate the impact of the alum on the potency.
  - If you have an adjuvant, you will likely have to use an in vivo assay to assess the potency because of the adjuvant impact in the in vivo system is not always clearly understood
  - The adjuvant can impact the quality of the antigen that is adsorbed to it

- Oncology Vaccines
  - Completely different risk / benefit paradigm than a prophylactic vaccine used in children