Elements of a framework for the evaluation of new vaccines

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February 23, 2022
Goals

Increase supply of vaccines that likely meet TPP criteria for effectiveness against severe disease

- Unless they confer major offsetting advantages, they should be as “variant-resistant” as current vaccines
- Under certain circumstances, a new vaccine could be considered for EUL based on an already-authorized comparator vaccine
- When these circumstances are not met, additional data would be needed prior to EUL

For this presentation, we consider demonstration of effectiveness, assuming that safety has already been addressed
Additional points

Recognizing that discussion of criteria for decision-making will be enhanced if there is a concrete proposal to discuss, we present a possible framework for evaluating new vaccines, based on scenarios that consider the effectiveness of the comparator against severe disease caused by circulating variants and the likelihood that humoral responses to a new vaccine will predict cellular responses.

We are discussing conditions under which there could be general agreement as to the pathway for EUL.

Conditions not currently presented in the draft framework may require further discussion, but for now, vaccines and studies not meeting these conditions would need to be considered for other types of clinical evaluations.
Some key questions

1. What is the effectiveness or efficacy of the comparator vs. severe disease caused by circulating VOC, relative to TPP criteria?

2. Is the predicted/likely CMI (or other relevant protective) response using the new vaccine likely to be similarly proportional to the humoral response vs. the comparator vaccine?
   - CMI responses appear to confer longer term protection and increase resistance of immune response to new variants

3. What is the breadth of antigenic composition relative to proposed comparator that is already EUL-authorized?
   - If new vaccine has less viral sequence, it may present fewer important cellular or non-neutralizing humoral epitopes
   - Any impact of 2-P mutation likely will be captured in magnitude of humoral response (so does not influence assessment of breadth)

Depending on careful/detailed assessment of these factors, proposed approaches to evaluating the new vaccine are presented.
<table>
<thead>
<tr>
<th>Key questions</th>
<th>Status of evidence in relation to key questions</th>
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<tbody>
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<td><strong>Scenario 1</strong></td>
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| What additional data do we need to authorize the new vaccine? | **Scenario 1** | NI Nabs to circulating variants | **Scenario 2** | Unambiguous superiority Nabs to circulating variants | **Scenario 3** | Super-Superiority Nabs to circulating variants | **Scenario 4** | Results as in Scenarios 1, 2, or 3 PLUS Additional clinical data* | **Scenario 5** | Additional clinical data (e.g. in deployment studies or human challenge data if feasible) |

| Comments on vaccine effectiveness | | | | | | | | Duration of effectiveness may not exceed that of comparator vaccine unless CMI response is better | Low CMI may lead to short duration of effectiveness |

**VACCINES THAT DON’T MEET ANY OF THESE CRITERIA WOULD NEED TO BE TESTED IN CLINICAL TRIALS**
Additional clinical data could take the form of:

- in-deployment studies, where timing of vaccination is randomized. This allows randomized comparisons between vaccinees and non-vaccinees.
- Controlled human infection model experiments, though it may be difficult to maintain up-to-date challenge stocks.
- Other studies?