Evaluation of the stability of the measles vaccine for use in Extended Controlled Temperature Conditions (ECTC)

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Introduction

• Challenges exist in reaching high levels of measles vaccination coverage; in the Democratic Republic of the Congo, low coverage at 76% prior to an outbreak in 2013 and a delayed reactive vaccination campaign contributed to a high 14% attack rate (Gignoux et al. 2018).

• MSF-OCB’s "Coup de Poing" measles strategy emphasizes quick response to outbreaks with targeted vaccinations at the epicenter followed by general vaccination for the remaining susceptible population.

• Strict cold chain conditions pose arduous operational challenges leading to barriers in effective vaccine delivery, particularly in remote, rural areas.

• In order to use thermostable vaccines to their full potential in a single excursion outside the cold chain, the WHO defined two major concepts:
  ❖ Extended controlled temperature conditions (ECTC): defines the stability studies needed to support such an approach. It can be used for the evaluation of different excursion scenarios (i.e. different temperature/duration combinations).
  ❖ Controlled temperature chain (CTC): defines specific programmatic requirements for the use of thermostable vaccines outside the cold chain that can tolerate a temperature of at least 40°C for at least 3 days.

• For vaccines to be eligible for this approach they need to: (1) show a robust stability profile when exposed to the defined excursion conditions and (2) undergo regulatory processes resulting in the relabelling of the vaccine for use under these conditions.

• Study objective: evaluate the stability of the measles vaccine according to the WHO guidelines on the stability evaluation of vaccines for use under Extended Controlled Temperature Conditions (ECTC).

Methods

• Secondary data analysis of measles vaccine stability data provided by the Serum Institute of India Private Limited (SIPL).

• Based on a WHO developed product release model that considers potency decay rates at different storage conditions.

• Vaccines released above an established minimum release potency (MRP) to ensure that at the end of their shelf-life in storage (2-8°C), potency remains above lower limit (LL) specifications.

• Stability evaluation for CTC/ECTC use assesses if remaining potency after exposure to high temperatures is above the required lower limit (LL).

Figure 1: Graphic representation of the WHO product release model for ECTC evaluation*

Table 1: Product release model parameters

<table>
<thead>
<tr>
<th>Period</th>
<th>Temperature</th>
<th>Batches (n)</th>
<th>Stability data: time points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shelf-life</td>
<td>2-8°C</td>
<td>Measles vaccine (3)</td>
<td>Initial, 3, 6, 9, 12, 18, and 24 months</td>
</tr>
<tr>
<td>(24-months)</td>
<td></td>
<td>MR vaccine (3)</td>
<td></td>
</tr>
<tr>
<td>2.9 days</td>
<td>40°C</td>
<td>MR vaccine (9)</td>
<td>Initial, 3, 6, 12, and 18 days</td>
</tr>
<tr>
<td>5 days</td>
<td>37°C</td>
<td>Measles vaccine (12)</td>
<td>Initial, 7, 14, 21 and 30 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MR vaccine (8)</td>
<td></td>
</tr>
</tbody>
</table>

Results

Figure 2: Product Release Model, CTC application (40°C)

• The lower limit potency level is reached before 3 days (2.9) when exposed to a temperature of 40°C.

Figure 3: Product Release Model, ECTC application (37°C)

• The lower limit potency level is reached at 5 days when exposed to a temperature of 37°C.

Discussion

• The measles vaccine maintained potency above the lower limit at 37°C for 5 days, meeting ECTC criteria.

• The vaccine did not satisfy the requirements necessary for CTC classification as the lower limit potency threshold is reached before 3 days at 40°C.

• This study confirms the potential for the measles vaccine to be used in an out-of-cold-chain strategy in its monodose presentation.

• For multidose presentations and in the absence of preservatives, more studies are needed to explore other key parameters, namely the risk of microbial contamination.

• The vaccine meets ECTC regulatory requirements. This data needs to be submitted by the manufacturer to the regulatory authority for approval before field use.