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

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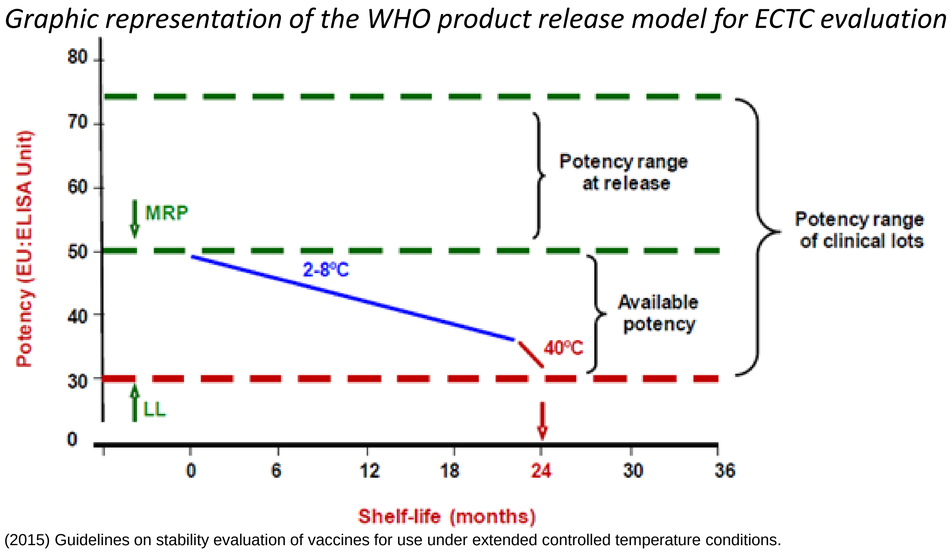
Introduction

- 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 (SIIPL).
- 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**



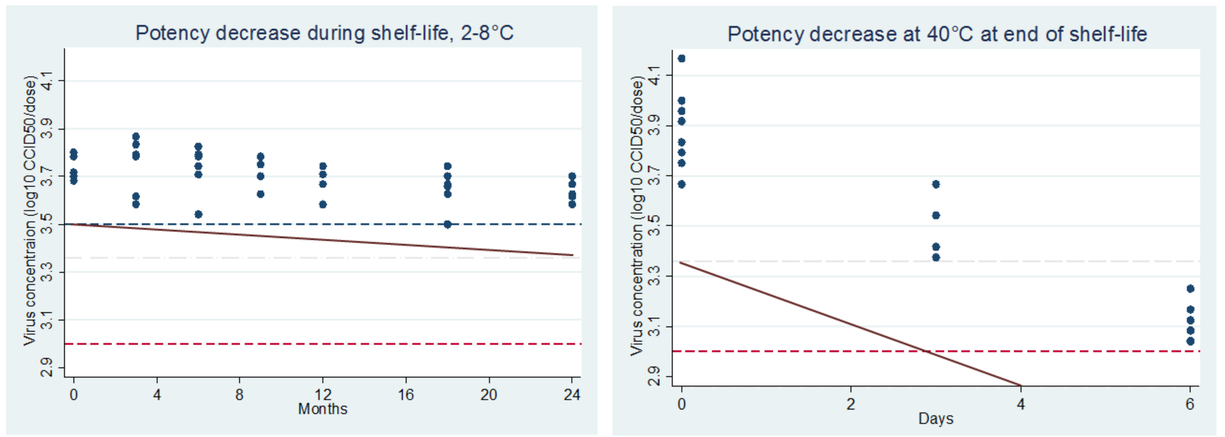
* From: WHO (2015) Guidelines on stability evaluation of vaccines for use under extended controlled temperature conditions.

Table 1: Product release model parameters

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

Results

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

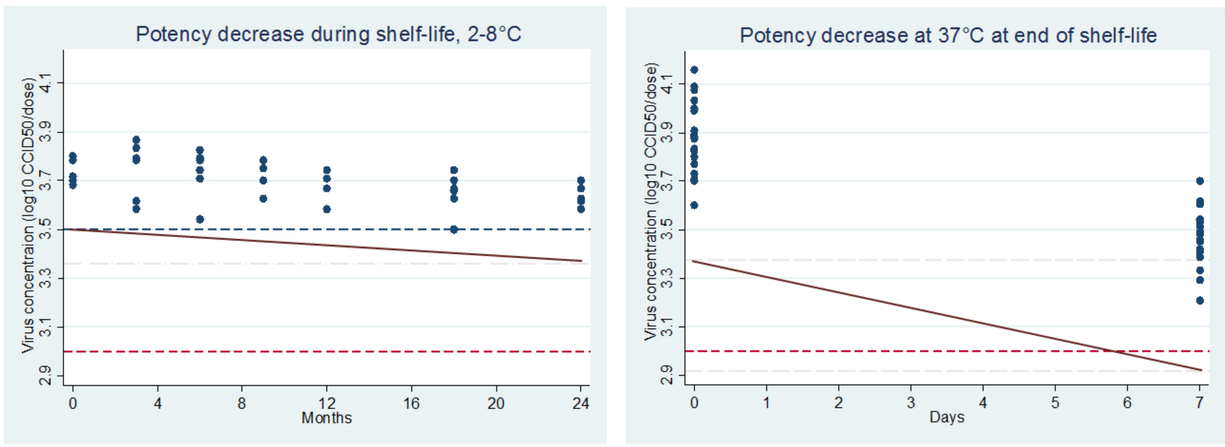


Assumptions:

MRP= 3.5	Decay slope at 2-8°C= -0.0052	Decay slope at 40°C=0.1266
Assay precision= 0.055	SE decay slope at 2-8°C= 0.0015	SE decay slope at 40°C=0.0085
α=0.05		

- 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)



Assumptions:

MRP= 3.5	Decay slope at 2-8°C= -0.0052	Decay slope at 37°C=0.0607
Assay precision= 0.055	SE decay slope at 2-8°C= 0.0015	SE decay slope at 37°C=0.0062
α=0.05		

- 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.