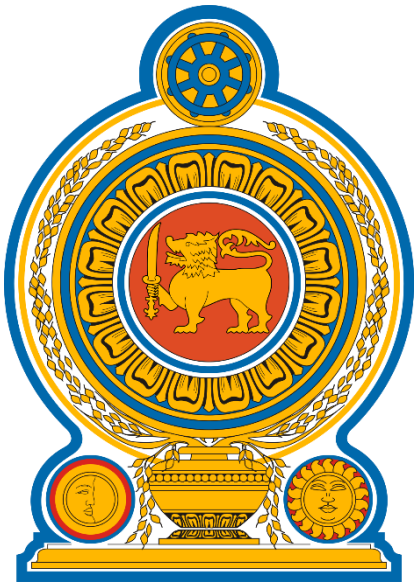

# GUIDELINE ON REGISTRATION OF VACCINES

OCTOBER 15, 2019

NATIONAL MEDICINE REGULATORY AUTHORITY
No.120, Norris Canal Rd, Colombo 01000, Sri Lanka

# GUIDELINE ON REGISTRATION OF VACCINES

**CONTENTS**



## 1. INTRODUCTION

A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters. (WHO).

## 2. SCOPE

National Medicines Regulatory Authority (NMRA) established under NMRA Act No 05 2015 to ensure that the medicines to the public meet the required standards of quality, safety, efficacy. Marketing authorization is one of the mandatory and important regulatory requirement.
This guideline is applicable to registration of all vaccines. The quality safety and efficacy of these products is assured through the requirements as described in this guidance document.
This documentation shall be read in conjunction with the current laws and regulations controlling medicines in Sri Lanka and guidelines for registration of medicines published by NMRA. The written laws shall take precedence over this guidance document in any event of discrepancy.

**Center for preregistration sample testing**
NCL Sri Lanka (MRI) is the prevailing body that is responsible for preregistration sample testing facility for vaccines

**Center for lot release**
NCL Sri Lanka (MRI) is the prevailing body that responsible for carried out Lot release process for vaccines as per NTP

## 3. ABBREVIATIONS

AEFI Adverse Events Following Immunization
CTD Common Technical Document
MRI Medical Research Institute
NCL National Control Laboratory
NMRA National Medicines Regulatory Authority
NRA National Regulatory Authority
NTP National Testing Policy
PMS Post Marketing Surveillance
SLMC Sri Lanka Medical Council
SLP Summary Lot Protocol
PHSRC Private Health Services Regulatory Council
SOP Standard Operating Procedure
WHO World Health Organization

## 4. REQUIRED DOCUMENTATION

Documents which are common for both medicines and vaccines should be submitted according to guideline on registration of medicines. This document includes required specific information required for vaccines.
1. Summary lot protocol (SLP) of production and quality control testing
The SLP of the product should contain all relevant details concerned with the manufacturing of the batch of vaccine. It should be made for each batch of the vaccine. This should contain detailed

information on manufacture and quality control of master seeds, working seeds, working cell banks, media, control cell cultures, single harvest, bulk, final bulk, final lot and final product.
Summary protocols should be prepared according to the WHO formats. The information to be included in the SLP is given in table 1. The protocol supplied by the manufacturer should include all appropriate production and control steps. Results of tests are required. Specifications of each test and dates when the tests were performed should also be included.
The SLP should be submitted for four batches.

**Table 1: Information to be included in the summary lot protocol**

| | Item | Essential Information to cover |
|---|---|---|
| 1 | Identity of manufacturer | Name of manufacturer |
| | Site(s) of manufacturing | Site of manufacturing for each bulk, final bulk and final Product |
| 3 | Name and lot number | Name and lot numbers of the final products, bulk, final bulk and the diluent if applicable |
| 4 | Lot size | Volume, number of doses and type of container |
| 5 | Expiry dates | For each starting material, intermediates, final bulk and final product |
| 6 | Dates of manufacturing | For each critical starting material (e.g. seed lots, cell banks, starting materials of animal origin etc.), intermediate, final bulk and final product |
| 7 | Flowchart | Flowchart for traceability of the manufacturing process for major components, including lot numbers |
| 8 | Strains and cell substrates | Name, seed lot number, passage number |
| 9 | Manufacturing process | Each production process (such as cultivation, purification, inactivation), the methods of quality-control tests as well as their release specifications and the results obtained; the lot number of intermediates and their size/volume, storage conditions |
| 10 | Formulation | Amount of active components in the final formulations, with the lot numbers and volumes of bulk concentrates; storage conditions |
| 11 | Quality control tests | •actual results of tests on critical starting materials, intermediates, final bulk and final product and the specification; |

| | | |
|---|---|---|
| | | •provide the starting date of the test, method, and a list of reference preparations, standards, critical reagents and their qualification status, plus the performance of relevant reference preparations, standards and internal controls, such as results of assay validity criteria (e.g. slope, intercept, linearity, 50% end-points, results of internal controls, challenge doses);<br>•provide statistical results, such as mean, geometric mean, standard deviation, 95% confidence intervals, etc., if applicable;<br>•include results of failed tests or note invalid tests if a test has been repeated |
| 12 | Filling, labeling and packaging | Sites, dates and details of equipment used |

The format and content of the summary lot protocol should be approved by the NCL during the registration process.

In situations where any changed done to the approved production process, the format of the protocol can be amended with the prior approval of NMRA. Such an approval should be recorded in the registration dossier and it is the responsibility of NMRA to inform the NCL and the Local agent about the approval.

2. **Manufacturing process and formula/ Master formula-**

**A**. Documents related to validation of processes and qualifications of equipment / devices and relevant SOPs.

B. Complete manufacturing formula should be submitted with description of each step with flow chart

1. Flow plan of manufacturing facility
2. Master seeds – certificate from NRA
4. Working seed – passaging, antigen content
5. Control cell cultures – testing for extraneous agents
6. Inoculation
7. Incubation
8. Harvesting – single harvest
9. Purification
10. Mixing process of combined vaccines
11. Bulk preparation
12. Final lot
13. Final product

3. Lot release certificate issued by the NRA / NCL of the manufacturing country (If filling and packaging of vaccine done in a separate country, lot release certificate from NRA / NCL of filling country also should be submitted).

4. Certificate of analysis of finished product

5. Certificate of analysis of diluent if applicable

6. The package information leaflet

**7. Clinical trial data & PMS data**

Detailed report on clinical trial should be submitted in format of module 5 of CTD. If it is a new application, PMS data from country of manufacture should also be submitted. If the application is for renewal of registration of a vaccine, PMS data of Sri Lankan market should be submitted in accordance with the format provided by the NMRA (Annex 1)

**8. List of countries**

List of countries where this particular vaccine is registered and list of countries where this vaccine registration is revoke should be submitted

**9. Prior registration check list**

Filled and signed prior registration checklist should be submitted as per Annexed 2

**ANNEXURE 1**

**Post Marketing Surveillance of Vaccines**
**Monthly Reporting Form**
**Name of the hospital:** Overall results

**Date:** **Month:** **Year:**

| Serial Number | Date of vaccination | Age of the vaccine (client) | Medical officer (prescriber) | Contact details of the medical officer | Type of the vaccine | Dose | Batch no./Lot no. | Expiry date | Type of the adverse reaction | Time duration between vaccination & occurrence of first symptom | Outcome recovered/ recovering | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | |

**Name & address of the local agent:**

**Type of the vaccine (1):**
**Total amount of the vaccine distributed:**
**No of Syringes:** ……. **No. of doses:** ……

**ANNEXURE 2**

**Prior registration checklist on vaccine quality and safety**

| | | Yes | No | Comment |
|---|---|---|---|---|
| 1 Vaccine storage and distribution plan | | | | |
| 1.1 | Vaccine storage facility at supplier level | | | |
| | 1.1.1 Availability of dedicated vaccine storage facility at (a) $2^0C$-$8^0C$<br>(b)- $20^0C$ | | | |
| | 1.1.2 Availability of temperature monitoring devices<br>(a) Thermometer<br>(b) Data lodger<br>(c) Freeze Tag | | | |
| | 1.1.3 Availability of a trained designated person for daily monitoring of temperature and cold chain | | | |
| | 1.1.4 Availability of vaccine carriers/Igloo to transport vaccine to sales outlets/Private Hospitals | | | |
| | 1.1.5 Availability of written vaccine distribution plan | | | |
| | 1.1.6 Availability of system to monitor maintenance of cold chain at sales outlet/Private Hospitals | | | |
| 1.2 | Vaccine distribution plan : essential components | | | |
| | 1.2.1 Vaccine will be sold/delivered *only* to authorized sales outlets/private Hospitals which are registered under NMRA/PHSRC. | | | |
| | 1.2.2 Vaccine will be sold /delivered *only* to sales outlets /private clinics where a dedicated refrigerator is available for vaccine storage. | | | |
| | 1.2.3 Vaccine will be sold/delivered *only* to sales outlets /private clinics where temperature monitoring devices are available (thermometer, Freeze tags, Data lodger) | | | |
| | 1.2.4 Vaccine will be sold/delivered *only* to sales outlets /private clinics where temperature monitoring records are available | | | |
| | 1.2.5 Vaccine will be sold/delivered *only* to sales outlets /private clinics where trained person(s)* to handle vaccine is/are available | | | |
| | 1.2.6 Vaccine will be sold/delivered *only* to private hospitals where SLMC registered medical officer is/are available | | | |

| | | | | |
|---|---|---|---|---|
| | 1.2.7 Vaccine will be sold/delivered *only* to private hospitals where a Register of all vaccine recipients are maintained | | | |
| | 1.2.8 Vaccine will be sold /delivered *only* to private hospitals from where regular return on AEFI data are sent to the MOH of the area. | | | |
| 2 Vaccine sales and safety information | | | | |
| 2.1 | Supplier shall send a quarterly return to NMRA with copy to Chief Epidemiologist, that include following sales information | | | |
| | 2.1.1 number of doses imported | | | |
| | 2.1.2 number of doses distributed | | | |
| | 2.1.3 number of doses dispensed by sales outlets/clinics | | | |
| 2.2 | Supplier shall send a quarterly return to NMRA with copy to Chief Epidemiologist on Post Marketing Surveillance (PMS) data | | | |
| | 2.2.1 PMS data from global | | | |
| | 2.2.2 PMS data from in country | | | |
| 3 Commercial Advertisement | | | | |
| | 3.1 Supplier agrees that *NO* commercial advertisement (both printed and electronic form) will be developed or/and distributed, making any comparison on quality and safety of vaccines used in the National Immunization Programme in Sri Lanka | | | |
| | 3.2 Supplier agrees that *NO* commercial advertisement (both printed and electronic form) will be developed or/and distributed, directly or indirectly affecting the public confidence on vaccines used in the National Immunization Programme in Sri Lanka | | | |
| | 3.3 Supplier agrees that *NO* direct or indirect commercial promotion of registering vaccine is done among medical and paramedical personnel | | | |

*Competence on vaccine cold chain maintenance is an essential part to ensure vaccine safety and quality in the private sector, as being practiced in the national immunization programme. Training on cold chain maintenance and vaccine safety is therefore necessary and supplier is responsible to facilitate the training need with the support from the Epidemiology Unit.

## 5. REFERENCE:

**http://www.who.int/topics/vaccines/en/**

## 6. FEEDBACK

6.1 Staff and customers may provide feedback about this document by emailing info@nmra.gov.lk.