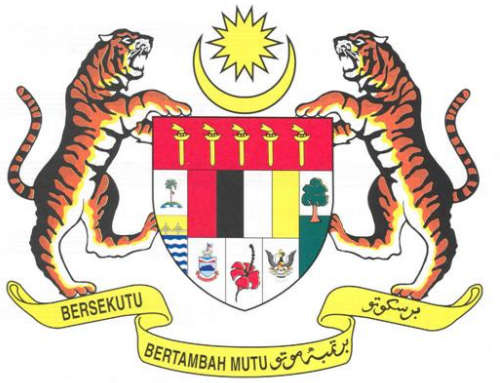

NATIONAL PHARMACEUTICAL REGULATORY AGENCY
MINISTRY OF HEALTH MALAYSIA

GUIDANCE DOCUMENT FOR VACCINES LOT RELEASE IN MALAYSIA

Third edition – Revised December 2016

GUIDELINE HISTORY

No.	Description of amendment	Effective date
1	First publication	1 July 2014
2	Revision of Guideline for Vaccine Lot Release First edition – July 2014	1 April 2015
3	Revision of Guideline for Vaccine Lot Release Second edition – April 2015	1 December 2016

GUIDANCE DOCUMENT FOR APPLICANTS: INFORMATION AND SUBMISSION REQUIREMENTS FOR VACCINES LOT RELEASE

National Pharmaceutical Regulatory Agency

Ministry Of Health Malaysia

December 2016

NATIONAL PHARMACEUTICAL REGULATORY AGENCY (NPRA)
MINISTRY OF HEALTH MALAYSIA

VISION:

TO BE A WORLD RENOWNED REGULATORY AUTHORITY FOR MEDICINAL PRODUCTS AND COSMETICS.

MISSION:

TO SAFEGUARD THE NATION'S HEALTH THROUGH SCIENTIFIC EXCELLENCE IN THE REGULATORY CONTROL OF MEDICINAL PRODUCTS AND COSMETICS.

OBJECTIVE:

TO ENSURE THAT THERAPEUTIC SUBSTANCES APPROVED FOR THE LOCAL MARKET ARE SAFE, EFFECTIVE AND OF QUALITY AND ALSO TO ENSURE THAT COSMETIC PRODUCTS APPROVED ARE SAFE AND OF QUALITY.

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TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS

BCG	Bacillus Calmette-Guérin (Tuberculosis Vaccine)
CQC	Center for Quality Control
CCL	Center for Compliance and Licensing
CDCR	Control of Drugs and Cosmetic Regulation 1984
DRGD	Drug Registration Guidance Documents
DPT	Diphtheria – Tetanus – Pertussis Vaccine
DT	Diphtheria – Tetanus Vaccine
EDQM	European Directorate for the Quality of Medicines & HealthCare
HepA	Hepatitis A Vaccine
HepB	Hepatitis B Vaccine
Hib	Haemophilus Influenzae Type B Vaccine
NCL	National Control Laboratory
NNC	Notification of Non-Compliance
NPRA	National Pharmaceutical Regulatory Agency
NRA	National Regulatory Authority
PRH(s)	Product Registration Holder(s)
SOP	Standard Operation Procedure
TRS	Technical Report Series
TT	Tetanus Toxoid Vaccine
VLR	Vaccine Lot Release
WHO	World Health Organisation

GLOSSARY

Applicant (product registration holder): The company or corporate or legal entity in the field of pharmaceuticals whose name the marketing authorisation has been granted. This party is responsible to all aspects of the product, including quality and compliance with the conditions of marketing authorization. The authorised holder must be subjected to legislation in the country that issued the marketing authorisation, which normally means being physically located in that country (1)

Combination vaccine: Vaccine with more than one antigen, combined in a single injection, e.g DPT vaccine combining diphtheria, pertussis and tetanus antigens (2)

Licensed importer: A person to whom an import license has been issued under Regulation 12, CDCR 1984 (3)

Licensed wholesaler: A person to whom a wholesaler's license has been issued Regulation 12, CDCR 1984 (3)

Lot: A defined quantity of starting material, packaging material, or product processed in a single process or series of processes so that it is expected to be homogeneous. It may sometimes be necessary to divide a lot into a number of sub- lots, which are later accumulated to form a final homogeneous lot. In continuous manufacture, the lot must correspond to a defined fraction of the production, characterised by its intended homogeneity. The lot size can be defined either as a fixed quantity or as the amount produced in a fixed time interval (4)

Lot release: The process of NRA/ NCL evaluation of an individual lot of a licensed vaccine before giving approval for its releasing onto the market (4)

Lot summary protocol: A document summarising all manufacturing steps and test results for a lot of vaccine, certified and signed by the responsible person of the manufacturing company (4)

Monovalent vaccine: A monovalent vaccine contains a single strain of a single antigen, e.g. Measles vaccine (2)

Non-compliance: Failure or refusal to comply with a standard or a set of limits (4)

NRA/ NCL: The NRA/ NCL taking the responsibility for regulatory oversight of a product for the critical regulatory functions defined by WHO, including independent lot release. Usually it is the country of manufacture unless specific agreements exist within defined territories such as in European Union where the 'country' of manufacture is the European Union and the activity of the responsible NRA/ NCL is designated from among the Member States (4)

Polyvalent vaccine: A polyvalent vaccine contains two or more strains/serotypes of the same antigen, e.g. Oral Polio Vaccine (2)

Prequalified vaccine: A vaccine that has been approved as acceptable, in principle, for purchase by United Nations agencies, such as WHO, after full assessment of all procedures involved in its production. The purpose of the assessment is to verify that prequalified vaccines: (a) meet the specifications of the relevant UN agency; and (b) are produced and overseen in accordance with the principles and specifications recommended by WHO, for good manufacturing practice (GMP), and for good clinical practice (GCP). This is to ensure that vaccines used in national immunisation services in different countries are safe and effective for the target population at the recommended schedules and that they meet particular operational specifications for packaging and presentation (4)

Reference country: The reference country for Malaysia is listed as per the latest version of Drug Registration Guidance Document by National Pharmaceutical Regulatory Agency (1)

1.0 INTRODUCTION

Vaccine is an antigenic substance that is administered into human intended to produce immunity to a disease by stimulating the production of antibodies. It is classified into live attenuated vaccines, inactivated vaccines, toxoid vaccines, sub-unit vaccines, polysaccharide vaccines, conjugated vaccines and recombinant vaccines. Production of vaccine is complex, arduous and requires a mastery of multiple technologies. Therefore, strict quality control and monitoring at every stage of process are mandatory in order to eliminate or reduce the risk due to production failures.

This guidance document is intended to facilitate local stakeholders to understand and meet the requirements for vaccine lot release in Malaysia.

1.1 General Overview of Vaccine Lot Release

Vaccine is a biological product used in healthy populations. It is given in a mass population, involving healthy babies and young children. Vaccine is complex in nature and more variable than chemically synthesised drug. The challenges in producing consistent lots of vaccines have raised doubts toward safety of vaccines. Different lot of vaccine is developed from inherently variable biological source and may cause deleterious effects such as reversion to virulence or toxicity or loss of immunogenicity. Since these effects may not be detected immediately after administration, major consequences may arise because vaccinations involve large number of healthy persons. Moreover, with the increasing number of people having doubts with the safety and success of national immunisation programme, any problems regarding the safety issues of vaccine would further tarnish the public trust on the public health strategies.

In addition to the manufacturing complexity, proper storage condition and efficient supply chain management must be ensured to preserve the sensitivity and limited shelf life properties of vaccine.

For these reasons, a careful independent review of manufacturing and quality control data on every lot is necessary before it is marketed. This is to ensure the consistent quality of manufactured lots.

Each vaccine lot is subject to the lot release programme before it is released onto the market. The PRH or importer must submit relevant documents or samples to NRA for independent assessment. Manufacturers must ensure that every new lot of vaccine is identical in its specific characteristics as outlined in the approved marketing authorisation.

Lot release programme will enable NRA to ascertain the safety and effectiveness of every lot of vaccines produced. Upon approval from the NRA, a formal release letter or certificate will be issued to allow release onto the market.

Independent assessment of vaccine can be based on:

a) review of manufacturers' summary protocols, which include manufacturing and testing data for each manufactured lot of the product
b) recognition/ acceptance of lot release certificate from responsible National Regulatory Authority
c) assessment of cold chain system monitoring
d) testing that is independent of the manufacturers' quality control testing

These approaches are not mutually exclusive and may be product-specific. Where appropriate, strategy for each particular vaccine shall be established by taking into consideration aspects such as the nature of vaccine, the post- market experience including production history and safety profile.

1.2 Guiding Principles

Our main intention is to safeguard public health and their well-being. The lot release programme provides an additional monitoring on each newly manufactured lot of vaccine. The approach employed in this programme is based on the recommendations by World Health Organisation (WHO).

1.3 Scope

This guideline is focused on registered imported vaccines for human use. This document is intended to provide guidance to vaccine PRHs, importers and wholesalers.

The content of this guideline will be reviewed and amended accordingly in the future for locally produced vaccine.

1.4 Scientific Guidelines Applicable to Vaccines Lot Release

Guidelines for Independent Lot Release of Vaccines by Regulatory Authorities and Technical Report Series (TRS) for all vaccines are available at WHO website: *http://www.who.int/*.

1.5 Implementation Timeline:

The vaccine lot release was implemented according to a phased timeline established by National Pharmaceutical Regulatory Agency (NPRA). The implementation was conducted in 2 phases as follow:

a) Pilot study: Vaccine (either combination or single antigen vaccine) which consists of Bacillus Calmette-Guérin (BCG), Diphtheria, Tetanus, Pertussis (DTP), Hepatitis B (HepB), Haemophilus Influenzae Type B (Hib), Polio and Human Papillomavirus (HPV). – Effective on 1st July 2014

b) Full implementation: Other antigens (either combination or single antigen vaccine) that are not stated in Phase 1 such as Hepatitis A (HepA), Influenza, Measles, Rubella, Rabies, Yellow Fever, Typhoid, Japanese Encephalitis, Varicella, Rotavirus, Zoster, Cholera, Meningococcal, Pneumococcal and others. – Effective on 1st January 2015.

Under both phases, monitoring of cold chain system is mandatory before releasing the vaccines onto the market.

2.0 GUIDANCE FOR IMPLEMENTATION

2.1 General

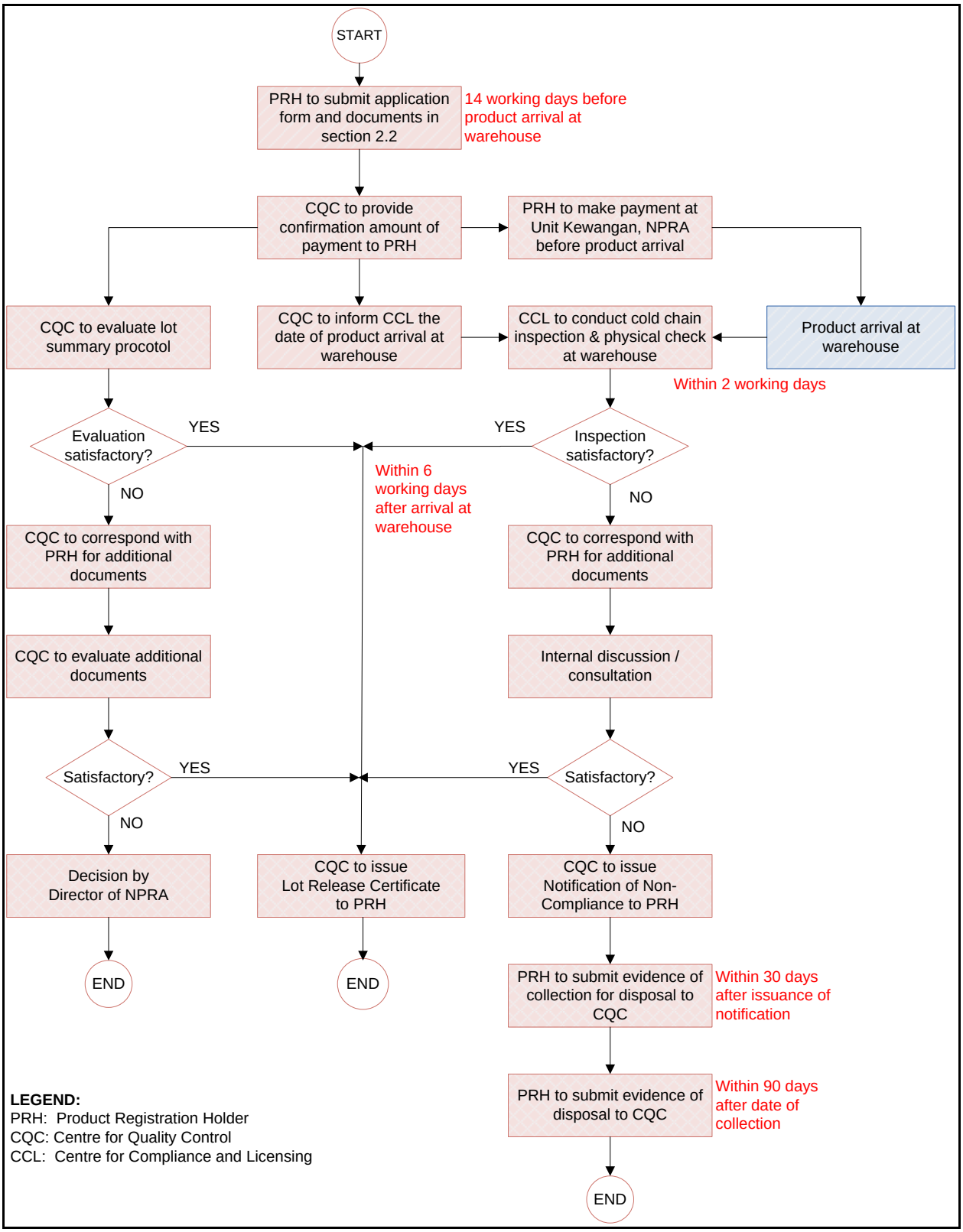
This guideline is largely based on the recommendation outlined in the Guidelines for Independent Lot Release of Vaccines by Regulatory Authorities (4). The lot release approaches for registered imported vaccines in Malaysia include:-

a) Review of manufacturer's summary protocol based on product dossier which has been approved by NPRA during product registration,
b) Review of cold chain system monitoring and appropriate data e.g. thermal cycling studies and shipping validation data which have been evaluated.

The Process Flow 1 diagram (below) illustrates the processes involved vaccines lot release. The process will involve the following parties:

a) Applicants (PRH)
b) National Pharmaceutical Regulatory Agency (NPRA)
c) Importers and
d) Wholesalers.

Process Flow 1: VACCINE LOT RELEASE PROCESS



General Procedure of Vaccine Lot Release in Malaysia:

i. Applicant submits application form (refer to Appendix 1) and documents (refer to section 2.2) via email to CQC (vaccineCQC@npra.gov.my).
ii. NPRA will response to the email by providing confirmation on the amount of fee to be paid. Please refer to section 2.11.1 of the guideline for further details on fees.
iii. Before product arrival, applicant makes payment to NPRA.
iv. Evaluation of summary protocol is conducted.
v. Within 2 working days after the arrival of vaccines at warehouse, NPRA's officer will conduct cold chain inspection and verify physical appearance of the vaccines.
vi. NPRA will issue lot release certificates if all the requirements have been fulfilled, within 6 working days after product arrival at warehouse.
vii. If the requirements are not met, NPRA will issue notification of non-compliance to reject the vaccines.
viii. In the event of non-compliance, it is the sole responsibility of the PRH to ensure proper safe disposal of the vaccines. A copy of collection for disposal documentation shall be sent to NPRA within 30 days after issuance of rejection and a copy of disposal documentation shall be sent to NPRA within 90 days after the collection date.
ix. Lot summary protocol for the same lot number being imported into the country at different times will not be evaluated again. However, cold chain inspection will still be conducted.
x. For cases stated in (ix), PRH should only submit the VLR application form, import packing list, airway bill and make payment for cold chain inspection

2.2 Guidance on the Submission of Documents

This guidance outlines the general requirement for documents submission. All the documents shall be written in *Bahasa Malaysia* or English only. Each document must be clearly tagged (indexed and labelled). Documents to be submitted are:

a) Application Form
b) Lot Release Certificate
c) Lot Summary Protocol
d) Certificate of Analysis (COA) for Finished Products
e) Importing Packing List
f) Airway bill.

Incomplete submission of documents may result in rejection of the application. Importing packing list and airway bill may be submitted two working days before product arrival.

2.2.1 Application Form

a) Application form is available in NPRA official website (refer to Appendix 1) and applicant shall use the same form without any amendment of the format
b) All sections shall be filled by applicant except section "For Office Use only"
c) Incomplete form will not be processed
d) The application form shall be submitted to CQC via email: vaccineCQC@npra.gov.my
e) The lot number (in final packaging) stated in the application form must be identical to the lot number on the lot summary protocol, lot release certificate and certificate of analysis.

2.2.2 Lot Release Certificate

Lot release certificate provided should be issued by the NRA from the country of origin.

In the event where the NRA does not provide a release certificate, and the vaccine is not a WHO prequalified vaccine, lot release certificate from any of the NPRA's eight (8) reference countries (United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan and Switzerland) will be accepted.

For list of WHO prequalified vaccine, kindly refer to WHO website: *http://www.who.int/*.

2.2.3 Lot Summary Protocol

The evaluation of the summary lot protocol will be based on dossier (Chemistry, Manufacture and Controls) which has been evaluated and approved by NPRA during product registration.

2.2.4 Certificate of Analysis (COA) for Finished Products

All release tests and its specification shall be the minimum requirement. Certificate of analysis for finished products may contain the following information:

a) name of manufacturer
b) product name, dosage form and strength
c) lot number (must be parallel to the lot number in the application form)
d) date of expiry
e) date of manufacture
f) list of tests
g) specification of tests
h) result of tests
i) approval from responsible person.

2.2.5 Importing Packing List

Applicant shall provide the details of importing packing such as:

a) date of shipment,
b) port of loading and discharge,
c) container numbers,
d) numbers and types of package,
e) gross weight (kg),
f) dimension Height x Width x Length (cm),
g) quantity,
h) description of goods and
i) other information related to the shipment.

The importing packing list must be submitted to CQC two (2) working days before the product arrival.

2.2.6 Airway bill (AWB)

For vaccine transported via air route, applicant shall provide the details of AWB such as:

a) Airway bill number
b) Airport of departure
c) Airport of destination
d) Flight number and date of arrival
e) Shipper's Name and Address
f) Consignee's Name and Address
g) Total number of packages
h) Description of goods

The airway bill must be submitted to CQC two (2) working days before the product arrival.

2.2.7 Criteria for requesting additional data

NPRA shall request additional data from PRH under conditions including but not limited to:

a) data provided are not reliable
b) insufficient information to support the evidence of the data (such as unavailability of raw data to support the results)
c) trending analysis data is out of normal trends (in this case, validation data for each parameter should be provided)
d) information of reference standard is not available (such as source of standard, procedure to produce standard and method used to standardise the standard)
e) NRA from the country of origin/ NPRA's reference countries does not issue lot release certificate or the vaccine is not a WHO prequalified vaccine.

Under condition (e), applicant shall provide all the testing raw data for the whole manufacturing process. Submission of requested data is mandatory for the first lot release application.

2.3 Guidance on Temperature Monitoring

Deviation of temperature or incorrect storage condition of vaccine may affect the quality, efficacy and subsequently the safety of vaccine. Hence, it is recommended that all vaccine products should be stored in their respective recommended condition at all times with continuous monitoring. Failure to show the traceability of temperature monitoring and appropriate storage condition may result in rejection of the entire lot of vaccine.

To facilitate the Cold Chain Inspection on arrival of product, suitable electronic temperature monitoring devices should be included in all shipments to document whether temperature limits have been exceeded. These devices shall serve as a quick reference to determine whether the shipment has been exposed to temperature at which products could have been damaged.

As temperature deviation could happen during transportation or redressing, PRH must submit relevant data and supporting document such as thermal cycling studies and shipping validation to justify temperature excursion for each product. The data must be sufficient to prove that the vaccine products remain stable at those storage conditions. All data must be submitted and will be evaluated by CCL. If the supporting documents or data provided is not sufficient to show evidence of product stability, the vaccine lot shall be rejected.

Please refer to the Guidelines on Good Distribution Practice (GDP) and Supplementary Notes for Management of Cold Chain Products/Material for further details on vaccine temperature monitoring.

2.4 Guidance on Shake Test

In the event of an adsorbed vaccine (DPT, DT, TT, Hep B, Hib liquid and/or combination of these) is suspected to be exposed to a freezing temperature, shake test shall be conducted by NPRA officers in NPRA laboratories. It is the responsibilities of the PRH to ensure the vaccine is transported to NPRA laboratories at an advised date by NPRA.

Vaccine to be used for shake test shall be taken based on a random sampling from the same lot of the affected vaccine, by NPRA. Vaccine used in the shake test shall not be returned to the PRH.

The detail of the Shake Test Protocol is available in Annex 2 of Guidelines on International Packaging and Shipping of Vaccines, WHO/IVB/05.23 December 2005.

2.5 Guidance on Non- Compliant

2.5.1 Non-compliant vaccine

In the event of non-compliant vaccine, the PRH shall ensure that the supply of the vaccine for the local use will not be affected.

The PRH shall ensure that non- compliant vaccines are not released onto the market and will be disposed in Malaysia. PRH shall provide appropriate proof of collection for disposal within 30 days after issuance of non- compliance notification and proof of disposal within 90 days after the date of collection.

2.5.2 Non-compliant product importer or wholesaler

Failure of importer or wholesaler to meet the requirement of Good Distribution Practice may result in revocation of import or wholesale license. In such cases, the PRH shall have a contingency plan to ensure that the supply of the vaccine for the local use will not be jeopardised.

2.6 Guidance on Exceptional Case

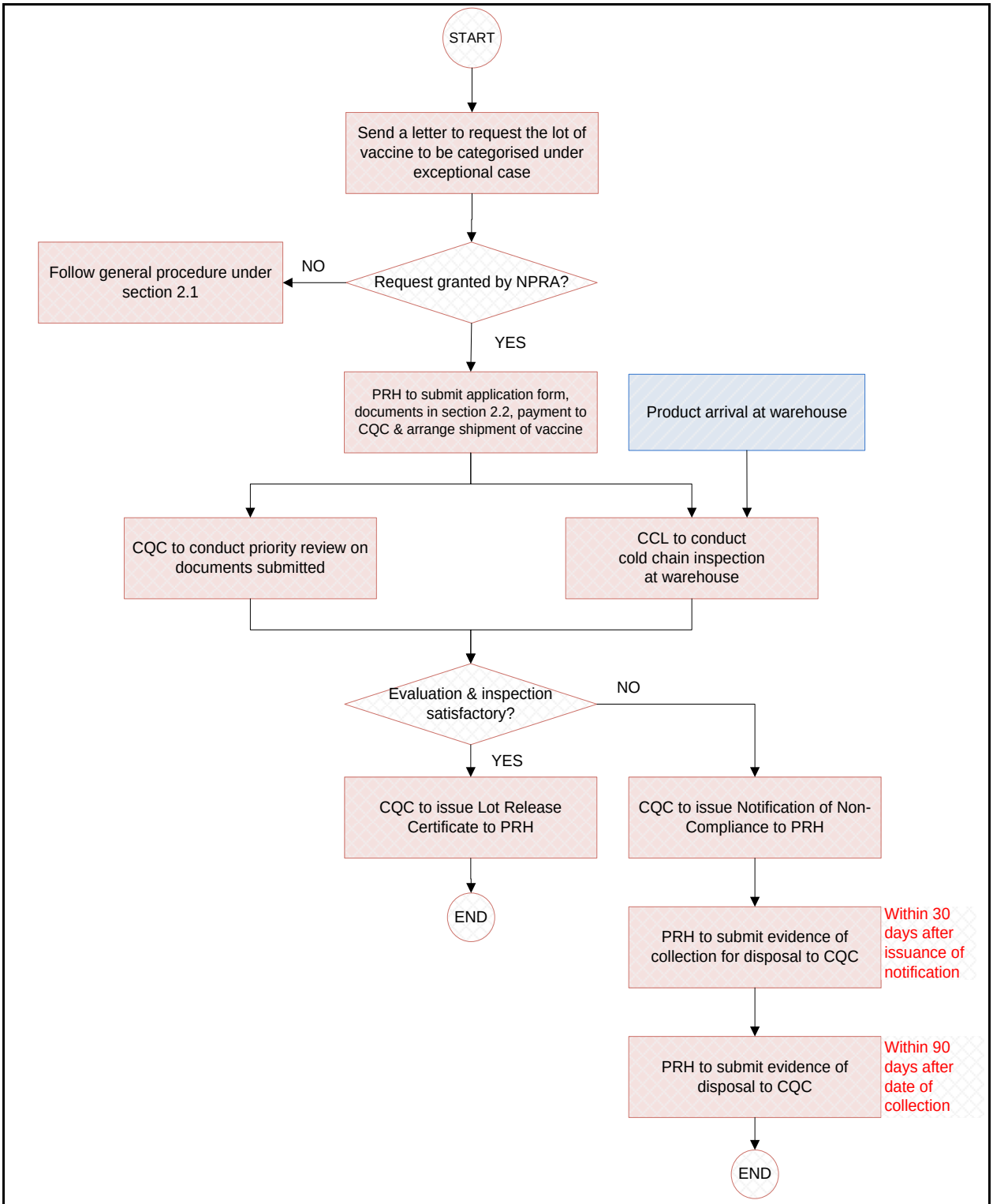
This guidance shall only apply to the emergence of crisis situation such as pandemic, epidemic, the shortage of product on the market or an urgent need due to changes in national health policy recommendation.

Exceptional case application shall be supported by related documents. It is not applicable as an alternative plan to support improper supply planning and handling of stock by applicant.

The Process Flow 2 diagram (below) illustrates the process of vaccines lot release system under exceptional case.

For other situations in which releases of vaccine lot need to be conducted immediately, it will be handled on case-to-case basis.

Process Flow 2: LOT RELEASE PROCESS FOR EXCEPTIONAL CASE



LEGEND:
PRH: Product Registration Holder
CQC: Centre for Quality Control
CCL: Centre for Compliance and Licensing
NPRA: National Pharmaceutical Regulatory Agency

General Procedure for Exceptional Case:

i. Applicant sends a requisition to Director of NPRA with accompanying justification for exemption case.
ii. If the request is accepted, applicant submits application form (refer to Appendix 1) and documents (refer to section 2.2) via email to CQC (vaccineCQC@npra.gov.my).
iii. NPRA will response to the email by providing confirmation on the amount of fee to be paid. Please refer to section 2.11.1 of the guideline for further details on fees.
iv. Before product arrival, applicant makes payment to NPRA.
v. Priority review on all the documents submitted will be conducted.
vi. Upon the arrival of vaccines at warehouse, NPRA shall conduct cold chain inspection.
vii. If the evaluation and inspection are satisfactory, NPRA shall issue lot release certificate.
viii. In the event of unsatisfactory evaluation or inspection of the respective lot, NPRA shall issue a non-compliance notification (NNC). A copy of collection for disposal documentation shall be sent to NPRA within 30 days of issuance of rejection. A copy of disposal documentation shall be sent to NPRA within 90 days after collection date.
ix. Lot summary protocol for the same lot number being imported into the country at different times will not be evaluated again. However, cold chain inspection will still be conducted.
x. For cases stated in (ix), PRH should only submit the application form, make payment for cold chain inspection and submit importing packing list.

2.7 Rejection Criteria for Vaccine Lot Release

Lot of vaccine shall be rejected under conditions including but not limited to:

a) decision from Director of NPRA based on the supporting document, comments from other NRA (if available) and summary from evaluator
b) failure to commit the requirement of cold chain management with no supporting data for temperature excursion
c) unseal of vaccine/quarantine vaccine without approval from NPRA
d) failure in physical appearance check during inspection with no supporting data
e) failure to provide additional data requested during evaluation or inspection
f) the product information leaflet and label are not updated accordingly or updated without NPRA's approval (approval for product variation by NPRA shall be received before the submission of lot release)

2.8 Guidance on Product Recall and Disposal

Please refer to the Guideline on Good Distribution Practice for further details on product recall and disposal.

2.9 Decision making

All the decisions made by NPRA are final and no appeal shall be allowed in any circumstances. The reason(s) of non- compliance will be clearly stated in the non- compliance certificate.

2.10 Timeline

Table 1 below shows the timeline for each activity in the lot release process.

Table 1:

Activity	Duration
Submission of application form and documents in section 2.2.1 – 2.2.4	14 working days before arrival of vaccines at warehouse
Payment for vaccine lot release	Within 14 working days before arrival of vaccines at warehouse
Submission of import packing list and airway bill (Section 2.2.5 and 2.2.6)	2 working days before arrival of vaccines
Conduct cold chain inspection	Within 2 working days after arrival of vaccines at warehouse
Issue of lot release certificate	Within 6 working days after after arrival of vaccines at warehouse
Submission of evidence of collection for disposal in the event of non-compliance	Within 30 days after issuance of notification of non- compliance
Submission of evidence of disposal in the event of non-compliance	Within 90 days after date of collection for disposal

2.11 Fees

Every application for vaccine lot release shall be charged.

Payment made shall **NOT** be **REFUNDABLE** once the application has been submitted and payment confirmed.

Applications without the correct fees will not be processed.

2.11.1 Types of fees

The fees imposed for vaccine lot release are shown in Table 2 and Table 3. The evaluation fee will be waived if the same lot of vaccine arrives at different times.

Table 2: Fee for West Malaysia:

Type of Vaccine	Cold Chain Inspection and Evaluation of Lot Summary Protocol	Cold Chain Inspection for Lot Summary Protocol has been evaluated
Monovalent vaccine	RM300/vaccine lot	RM200/vaccine lot
Polyvalent vaccine	RM500/vaccine lot	
Combination vaccine	RM1000/vaccine lot	

Table 3: Fee for East Malaysia:

Type of Vaccine	Cold Chain Inspection and Evaluation of Lot Summary Protocol	Cold Chain Inspection for Lot Summary Protocol has been evaluated
Monovalent vaccine	RM600/vaccine lot	RM500/vaccine lot
Polyvalent vaccine	RM800/vaccine lot	
Combination vaccine	RM1300/vaccine lot	

2.11.2 Mode of Payment

The processing fee and any other charges shall be paid in the form of cash/ credit card/ bank draft/ banker's cheque/ money order/ postal order made payable to **"Biro Pengawalan Farmaseutikal Kebangsaan"**.

3. REFERENCES

1. MALAYSIA. MINISTRY OF HEALTH MALAYSIA. (2014) *Drug Registration Guidance Document* 1st edition. National Pharmaceutical Control Bureau, 2014 [Online]. Available from: http://portal.bpfk.gov.my/index.cfm?&menuid=122 [Accessed: 7th May 2014].

2. Module 2 Types of vaccine and adverse reaction. In: *WHO Vaccine Safety Basics Learning Manual*. Geneva, World Health Organization, 2013. [Online] Available from: http://www.who.int/vaccine_safety/initiative/tech_support/ebasic/en/ [Accessed: 7th May 2014].

3. MALAYSIA. *Sales of Drug Act 1952: Control of Drugs and Cosmetic Regulation 1984: Regulation 2* (1984). [Online]. Available from: http://www.pharmacy.gov.my/v2/sites/default/files/document-upload/control-drugs-and-cosmetics-regulation-1984.pdf [Accessed: 7th May 2014].

4. Guidelines for independent lot release of vaccines by regulatory authorities. In: *WHO Expert Committee on Biological Standardization. Sixty-first report.* Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 978), Annex 2. [Online] Available from: http://apps.who.int/medicinedocs/documents/s21098en/s21098en.pdf [Accessed: 7th May 2014].

5. MALAYSIA. MINISTRY OF HEALTH MALAYSIA. (2013) *Guidelines on Good Distribution Practice 2nd edition.* National Pharmaceutical Control Bureau, 2013 [Online]. Available from: http://portal.bpfk.gov.my/index.cfm?&menuid=122 [Accessed: 7th May 2014].

6. Stanley A Plotkin, MD. *Vaccine Fact Book 2013*. United States; 2013

7. WHO good distribution practices for pharmaceutical products. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourty-forth report*. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 5. [Online] Available from: http://www.who.int/medicines/publications/TRS957_2010.pdf [Accessed: 7th May 2014].

4. APPENDIX

Appendix 1: Application Form for Vaccine Lot Release

VS/001A
Version 3
Effective Date: 01 November 2016

Agensi Regulatori Farmasi Negara (NPRA)
Kementerian Kesihatan Malaysia
Lot 36, Jalan Universiti, 46200 Petaling Jaya, Selangor.
No. Tel : 03-78835400
No. Faks : 03-79567075
Laman Web: http://npra.moh.gov.my
Emel Unit Kawalan Kualiti Vaksin: vaccinecqc@npra.gov.my
Emel Pemeriksa Rangkaian Sejuk : cc@npra.gov.my

VACCINE LOT RELEASE APPLICATION FORM

1. APPLICANT INFORMATION	
1.1 Name & Address of Product Registration Holder	
1.2 Name & Address of Importer	
1.3 Name & Adress of Warehouse	
1.4 Contact Person	
1.5 Contact no.	
2. VACCINE INFORMATION	
2.1 Name of vaccine as registered in Quest System	
2.2 Ingredients & strength	
2.3 Name of manufacturer	
2.4 Name of other manufacturer (If any)	

2.5 MAL no.	2.6 Lot no. of vaccine
2.7 Date of manufacture	2.8 Expiry date
2.9 Storage condition	2.10 Types of final container for vaccine ☐ Vial ☐ Prefilled syringe ☐ Ampoule ☐ Others; please specify _____
3. DILUENT INFORMATION (IF ANY)	
3.1 Name of diluent	3.2 Lot no. of diluent
3.3 Date of manufacture	3.4 Expiry date
3.5 Storage condition	3.6 Types of final container for diluent ☐ Ampoule ☐ Prefilled syringe

4. QUANTITY OF VACCINE IMPORTED		
4.1 Quantity in primary packaging	4.2 Quantity in secondary packaging	4.3 Total no. of doses per shipment

VS/001A
Version 3
Effective Date: 01 November 2016

5. TRANSPORTATION OF VACCINE	
5.1 Arrival date	**5.2 Transit point (if any)**
5.3 Route of transportation ☐ Air ☐ Ocean	**5.4 Mode of transportation** ☐ Active system ☐ Passive system

6. DOCUMENTATION	
6.1 Documents submitted	☐ Lot Summary Protocol ☐ Lot Release Certificate ☐ Certificate of Analysis of Finished Product ☐ Importing Packing List ☐ Air Way Bill / Sea Way Bill

7. REDRESSING / REPACKING/RELABELLING INFORMATION (ONLY APPLICABLE FOR MAL NO. WITHOUT SUFFIX -R)	
7.1 Do these product require redressing/repacking/ relabelling? ☐ Yes. Refer to 7.2 ☐ No	**7.2 Have you submitted a request letter to conduct ANY redressing/repacking for these products to the Regulatory Coordination Section, Centre for Product Registration (SKR PPP)?** ☐ Yes. Submission date: _____ ☐ No

The Malaysian Drug Registration Guidance Document defines redressing, repacking and relabelling as a manufacturing activity. Manufacturing of products without a valid manufacturing license is an offense under Control of Drugs and Cosmetics Regulations 1984 [Regulation 12(1)]

8. APPLICANT DECLARATION

I hereby certify that the above information given are true and correct as to the best of my knowledge. I understand that if any of the above information is found to be false or untrue or misleading or misrepresenting, I am aware that I may be held liable for it, this application will be rejected and any payments made will not be refunded.

Remarks		
Name	**Signature**	**Date**

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VLR Documents complete?	☐ YES ☐ NO. List of pending documents: ☐ LRC ☐ COA ☐ AWB/SWB ☐ Importing Packing List	**Received by, date & signature**
No. bil. SAB: Bil ( ) BPFK/PKK/16/01 **Date of issuance:**	**Amount:** ☐ RM200 ☐ RM300 ☐ RM500 ☐ RM1000	**Issued by, date & signature**
Date of payment received:	**Receipt no.:**	**Received by, date & signature**

5. LIST OF UPDATES

NO.	REVISION	UPDATES		REFERENCE
		SECTION/ APPENDIX	DETAILS	
1	April 2015	1.4	Removal of information on OCABR Guideline	Task Force Biological Lot Release Meeting No. 1/2015
2	April 2015	2.1 (b)	Removal of 'Acceptance of release certificate from NRA/NCL from country of origin'	Task Force Biological Lot Release Meeting No. 1/2015
3	April 2015	2.1 Process flow	Change of process flow	Task Force Biological Lot Release Meeting No. 4/2015
4	April 2015	2.2 (f) and 2.2.6	Include Airway Bill	Task Force Biological Lot Release Meeting No. 1/2015
5	April 2015	2.2.2	Ammend the link for list of WHO prequalified vaccine	Task Force Biological Lot Release Meeting No. 1/2015
6	April 2015	2.6	Include information on shake test	Task Force Biological Lot Release Meeting No. 2/2015
7	April 2015	2.9 Table 1	Revised timeline	Task Force Biological Lot Release Meeting No. 1/2015
8	April 2015	2.10.2	Removal of 'A separate bankdraft/banker's cheque/MO/PO is neccessary for each application lot'	Task Force Biological Lot Release Meeting No. 1/2015
9	April 2015	4.1 Appendix 1	Change of application form for Vaccine Lot Release to version 2 (Effective date 1 May 2015)	Task Force Biological Lot Release Meeting No. 5/2015

NO.	REVISION	UPDATES		REFERENCE
		SECTION/ APPENDIX	DETAILS	
10	December 2016	Title	Change of title from "Guidance Document and Guidelines for Vaccine Lot Release in Malaysia" to "Guidance Document for Vaccine Lot Release in Malaysia"	Task Force Biological Lot Release Meeting No. 6/2016
11	December 2016	Whole document	Change of name from "National Pharmaceutical Control Bureau (NPCB)" to "National Pharmaceutical Regulatory Agency (NPRA)"	Task Force Biological Lot Release Meeting No. 6/2016
12	December 2016	2.3	Include the requirement to use electronic temperature monitoring devices	Task Force Biological Lot Release Meeting No. 6/2016
13	December 2016	2.6	Include additional requirement for Exceptional case application	Task Force Biological Lot Release Meeting No. 6/2016
14	December 2016	Appendix 1	Change of application form for Vaccine Lot Release to version 3 (Effective date 1 December 2016)	Task Force Biological Lot Release Meeting No. 10/2016