NATIONAL VACCINES' LOT RELEASE GUIDELINES, BANGLADESH

NATIONAL DRUG CONTROL LABORATORY (NDCL)

Directorate General of Drug Administration (DGDA)
Health Service Division
Ministry of Health and Family Welfare (MOH&FW)
Government of the People's Republic of Bangladesh

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30.07.24	**03**	All changes are harmonized with current practice of NDCL, DGDA, The Drug and Cosmetics Act 2023 and WHO Guideline (Annex 2, TRS 978). DCR reference: DCR/QA/002/24

This guideline is harmonized with
Guidelines for independent lot release of vaccines by regulatory authorities (WHO Technical Report Series 978, Annex 2), Drug and Cosmetics Act-2023 and current regulatory practices of DGDA.

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List of Abbreviations

CoA	Certificate of Analysis
CoC	Certificate of Compliance
CoP	Chief of Party
DGDA	Directorate General of Drug Administration
GMP	Good Manufacturing Practice
IS	International Standard
LIMS	Laboratory Information Management System
LR	Lot Release
LRC	Lot Release Certificate
MA	Marketing Authorization
MOH&FW	Ministry of Health & Family Welfare
NCL	National Control Laboratory
NDCL	National Drug Control Laboratory
NRA	National Regulatory Authority
OOS	Out of Specification
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
SD	Standard Deviation
SLP	Summary Lot protocol
SOP	Standard operating procedure
TRS	Technical Report Series
UN	United Nations
WHO	World Health Organization

1. Introduction

Vaccine lot release (LR) conducted by regulatory authorities is part of the regulation of vaccines and involves the independent assessment of each individual lot of a licensed vaccine before it is released onto the market. This assessment is based, at a minimum, on the review of manufacturers' summary protocols. It may be supplemented by other documents, such as the release certificate from the responsible National Regulatory Authority (NRA)/National Control Laboratory (NCL), and in some circumstances, by an independent testing facility that is independent of the manufacturers' quality control (QC) testing.

The World Health Organization (WHO) provides support for LR programs through provision of written and measurement standards, strengthening NRAs' LR functions, and providing training. This document provides comprehensive guidance recommendations for LR of vaccines by the NRAs/NCLs of producing and procuring countries following regulations. It should be read in conjunction with the recommendations/guidelines for specific products, for example, recommendations for Bacille Calmette-Guérin vaccine; oral polio vaccine; measles, mumps, and rubella vaccine; diphtheria, tetanus, and pertussis vaccine; human papillomavirus vaccine; and rotavirus vaccines.

This guideline is intended to cover possibilities that address different circumstances related to LR. Independent LR involves confirmation that each lot meets the specifications in the approved Marketing authorization (MA) for the product. Under defined circumstances, laboratory testing by a National Drug Control Laboratory (NDCL) can provide added value to this confirmation. The need for testing should, however, be justified according to criteria as specified in this document, and the laboratory should operate under an appropriate quality assurance (QA) system. When independent laboratory testing is undertaken, NDCL should ensure that it is conducted according to the principles defined in this document. Testing under inappropriate conditions may generate inaccurate data and lead to misleading decisions. This guideline also highlights the importance of networking and work sharing among NRAs/NCLs.

The guideline is intended to serve as a guide for national requirements for LR.

2. Scope

This guideline focuses on vaccines for human use. However, general principles of this guideline can be applied for other biological products also.

This document provides guidance to the Directorate General of Drug Administration (DGDA), local vaccine manufacturers, MA holders, importers, and distributors with respect to the official LR program of DGDA. It may also be relevant to public health authorities such as the Expanded Program on Immunization (EPI).

3. Glossary

The definitions given below apply to the terms used in this guideline. They may have different meanings in other contexts.

Annual product quality review (APQR): A yearly report sent by manufacturers to the DGDA/NDCL that contains production data on bulk and final batches, test procedures and outcomes, the justifications for any recalls and corrective actions performed, and other significant post-market data.

Certificate of analysis (CoA): A document that contains all release tests and their specification based on the product MA file that has been evaluated and approved by DGDA during product registration.

Certificate of compliance (CoC): A document that certifies that a product or system meets the requirements of a safety regulation or standard.

Deviation: Departure from a standard or norm or from a set of limits.

Laboratory information management system (LIMS): A software system that automatically facilitates the management of samples, test results and associated data to improve lab productivity and effectiveness. A LIMS provides the standardization of workflows, procedures and tests, and also ensures control over the processes in the lab.

Lot: A predetermined quantity of raw materials, packing materials, or finished goods that are processed via one or more procedures with the goal of producing a homogeneous result. In continuous manufacturing, the lot must represent a specific portion of the production and be distinguished by the uniformity it is aiming to achieve. Either a predetermined number or the amount produced in a set amount of time can be used to define the lot size.

Sub-lot: A lot may occasionally need to be divided into smaller lots, which are then combined to create a larger, more homogeneous lot.

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

Lot release certificate (LRC): An official document that authorizes the release of a specific lot into the market.

Marketing authorization (MA): An official document issued by the competent NRA for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy, and quality.

Non-compliance: Failure or refusal to comply with a standard or a set of limits.

Out of specification (OOS): A result generated when a vaccine is tested and fails to meet a predefined specification**.**

Responsible NRA/NCL: The NRA/NCL takes the responsibility for regulatory oversight of a product for the critical regulatory functions defined by WHO, including independent LRs.

Usually, it is the country of manufacture unless specific agreements exist within territories, such as in the European Union, where the “country” of manufacture and the activity of the responsible NRA/NCL is designated from among the Members States.

Sampling: The operations designed to select a portion of a pharmaceutical product for a defined purpose. The sampling procedure should be appropriate to the purpose of sampling, to the type of controls intended to be applied to the samples, and to the material to be sampled. The procedure should be described in writing. All operations related to sampling should be performed with care, using proper equipment and tools. Any contamination of the sample by dust or other foreign material is liable to jeopardize the validity of the subsequent analyses.

Risk based approach: An NRA reliance approach that considers factors such as the type and source of products evaluated, the level of resources and expertise available in the NRA, the public health needs and priorities of the country, and opportunities for reliance.

Self-procured vaccine: A vaccine that is procured directly from a source outside the country without intervention of WHO/United Nations (UN) procurement programs.

Source material/ starting material: Any substance of a defined quality used in the production of a vaccine product but excluding packaging materials.

Summary lot protocol (SLP): (also called **lot summary protocol**): A document summarizing all manufacturing steps and test results for a lot of vaccine that is certified and signed by the person responsible at the manufacturing company.

Trend analysis: A technique to analyze data over time to identify patterns, trends, or changes in the QC data.

4. General Considerations

Vaccines are biological products administered to healthy populations. It could take years to determine the effects of utilizing subpar lots. Comparably, safety concerns pertaining to a certain lot might not be identified right away (within a few hours) following administration, and the consequences could be severe if healthy people receive a vaccination before an issue is identified (WHO,1992). For these reasons, before it is commercialized, a thorough independent examination of the production and QC data on each batch is required. Issues with vaccine quality directly affect public approval of immunization programs, thereby jeopardizing public health initiatives. As a result, before a lot is put on the market, it is crucial to ensure that its quality remains consistent.

Furthermore, vaccines and many of the tests applied to them are of a biological and complex nature and have an inherent potential for variability. Therefore, an independent review of critical data from each lot of vaccines is essential to assure the consistent quality of each manufactured lot.

Reference standards used in the testing of vaccines are also biological in nature and prone to the same issues of complexity and stability as the vaccines themselves. For new products, national standards, international standards (IS), or reference preparations are not always

available, and there may be limited data on the stability of in-house or working standards used. Independent review of data is necessary to gain confidence in the results of tests using these preparations.

DGDA has an independent laboratory NDCL for testing vaccines and an independent unit for LR of vaccines. LR is done based, at a minimum, on a thorough review and approval of the manufacturers' SLP with or without laboratory testing or through a decision of another reliable regulatory authority. All vaccine lots are released by NDCL/DGDA; however, in defined exceptional circumstances, such as a public health emergency, exemptions are allowed. The permitted circumstances and the procedures to be followed to ensure quality in the absence of LR should be covered by legal provisions (Drug and Cosmetics Act-2023, Section 67).

LR is part of the entire regulatory framework, which includes Marketing Authorization, Regulatory inspection, Licensing premises, Laboratory access and testing, Post-Market surveillance and control and Pharmacovigilance. DGDA and NDCL maintain an effective mechanism for interaction between each department and exchange of information among them.

This is a national guideline for LR of vaccines in Bangladesh. It explains comprehensive procedures from the submission of the vaccine lot for release to the issue of LRCs.

4.1 Legal and Related Documents

4.1.1 Drug and Cosmetics Act-2023 (Annex 3);

4.1.2 Gazette Notification by Ministry of Health and Family Welfare (MOH&FW) (Annex 4);

4.1.3 Drug Policy 2016; and

4.1.4 NRA Lot Release Committee (DGDA Office Order).

4.2 Consideration for Establishing Lot Release Procedures by DGDA/NDCL

NDCL/DGDA will follow one of the following approaches for conducting LR of locally and self-procured vaccines and vaccines procured through United Nation (UN) agencies:

4.2.1 Review of the summary protocol only;

4.2.2 Review of the summary protocol with independent testing (partial/selected testing);

4.2.3 Review of the summary protocol with independent testing (full testing);

4.2.4 Review of LRC of Country of origin in case Vaccine is produced from PQ source through UN procurement chain. Certificate of Compliance, instead of LRC, is issued in such case; and

4.2.5 Reliance/acceptance of LRCs from the responsible NRA/NCL.

The NDCL, DGDA will decide an appropriate strategy by taking into consideration the type of vaccine, the post-marketing experience (including production history and safety profile), and the availability of other independent evidence of product quality. Considering the highly variable nature of biological products, including vaccines, and the complexity of the test method, any further (repeat) testing will be carefully justified to avoid “false” OOS results, which then require extensive investigation and delay vaccine supply. In such case reliance approach will be availed.

For vaccines produced and authorized either for domestic use or for export, NDCL/DGDA will take responsibility for regulatory oversight of vaccine quality. The NDCL/DGDA will initially perform tests on selective consecutive batches of the vaccine until they ensure the quality of vaccines, have developed the NDCL’s confidence, and have carried out a critical review of the summary protocols. After confirmation of the consistency of the quality through testing the chosen parameters, release of further lots should include full or selected testing or no testing, depending on the nature of the product and established experience.

In case any of the manufacturers decides to toll manufacture a vaccine in any other country where it is not licensed, DGDA/NDCL will take full responsibility for regulatory oversight. However, co-operation with the NRA of the producing country is recommended.

4.3 Networking and Work Sharing

The Bangladesh NDCL, DGDA is an associate member of the WHO National Control Laboratory Network for Biologicals and WHO Rapid Alert System. DGDA will share any information or issues (as approved by national legislation/ guideline) that will be useful for other countries in the network. This helps to limit or eliminate unnecessary or repeat testing/evaluation already done by other countries.

Sharing test results can contribute to reducing the number of animals used for testing and can prevent samples being tested in laboratories that perform certain assays infrequently and may have problems in maintaining technical competence. Work sharing also enables the development of more complex and specialized methods through repetition of tasks, which provides a support network for problem solving.

NDCL/DGDA will take part in the capacity-building activities for countries in a regional laboratory network. A fully functional regional laboratory network is a long-term goal, but cooperation can begin in the short term by sharing scientific information and experiences with methodologies regarding the evaluation and release of different products. NDCL/DGDA will actively participate in the meetings organized by WHO to promote transparency and mutual confidence between the NRAs and NCLs.

5. Responsibilities of NDCL/DGDA and the Manufacturer in Lot Release

The quality, safety, and efficacy of medicinal products such as vaccines are the responsibility of the manufacturer. NDCL/DGDA will ensure that the quality, safety, and efficacy of a medicinal product, such as vaccines, are met.

The same requirements of regulatory oversight should apply to the production of vaccines whether they are intended for domestic use or export.

5.1 Responsibilities of NDCL/DGDA in Lot Release

DGDA will grant/issue the MA for vaccines and will be responsible for continued post-authorization monitoring. To carry out this monitoring, DGDA has established an NDCL for vaccine testing and a lot release committee comprising of experts on LR activities. These activities are specifically mentioned in the Drug and Cosmetics Act-2023.

Responsibilities of the NDCL/DGDA for issuing the LRC has been mentioned in legal provision (Drug and Cosmetics Act-2023). Timelines and other details should be defined in the in-house procedure. The manufacturer and relevant health authorities should be informed in the event of a delay.

The NDCL, DGDA have a procedure (NC-QA-GNL-006) to request adequate samples required for LR from manufacturers, when required. The procedure also describes lot identification and retention for future reference.

NDCL also has access to externally qualified laboratories with specialized facilities, equipment, and expertise.

NDCL is independent of the manufacturer and any other laboratory. NDCL does not share any staff or resources that can create conflict.

The NDCL, DGDA posts and regularly updates the mechanism for the independent LR procedure in DGDA website (dgdagov.info) in a clear and transparent way regarding requirements and timelines so that the process is completed smoothly and in a timely manner.

NDCL, DGDA provides information concerning the quality of products in question to the /NCL of an importing country upon request. Rules and procedures regarding confidentiality of information are maintained, and the data submitted by manufacturers and other NRAs are kept confidential unless agreed upon otherwise as per the defined procedure of NDCL, DGDA.

The NDCL, DGDA has the responsibility to ensure the release of assured quality vaccines whether they are used in the country or exported. The vaccines for local use and those for export should have the same level of quality.

5.2 Responsibilities of Applicant in NDCL/DGDA Lot Release

The applicant has the following responsibilities in terms of NDCL/DGDA lot release:

5.2.1 Collaborate with the NDCL/DGDA to develop the product summary protocol template when requested (the WHO summary protocol of each product could be used as the template).

5.2.2 Submit each manufacturing and control summary protocol.

5.2.3 If requested, submit samples in an appropriate condition, including packaging, leaflet, and label.

5.2.4 Assist DGDA and NDCL in technical transfer of testing methods, including training, wherever required.

5.2.5 Provide product-specific reagents and working reference materials with certificate, as needed.

5.2.6 Participate in collaborative studies in establishment of a national standard.

5.2.7 Work with DGDA/NDCL to resolve any discrepancy on test result work.

5.2.9 Take appropriate action on the issues related to any error/noncompliance/OOT.

5.2.10 Take appropriate action on any rejected lots according to good manufacturing practice (GMP) requirements.

5.2.11 Provide any documents, data (paper and electronic), or other information regarding the quality of the vaccine required by the NDCL/DGDA as per procedure (NC-QA-GNL-056).

5.2.12 Provide justification of any variation of test method used, for example, for in-vivo test in place of in-vitro test.

5.3 NDCL/DGDA Quality Management Systems

NDCL/DGDA has established a quality management system (QMS) to support LR activities that include the following key elements:

5.3.1 Trained and qualified personnel;

5.3.2 Adequate and calibrated equipment;

5.3.3 Management of records and documentation;

5.3.4 Identification and retention of samples (when applicable);

5.3.5 Use of validated test procedures and written procedures;

5.3.6 Internal and external audit systems and oversight procedures;

5.3.7 Health, safety, and environmental compliance;

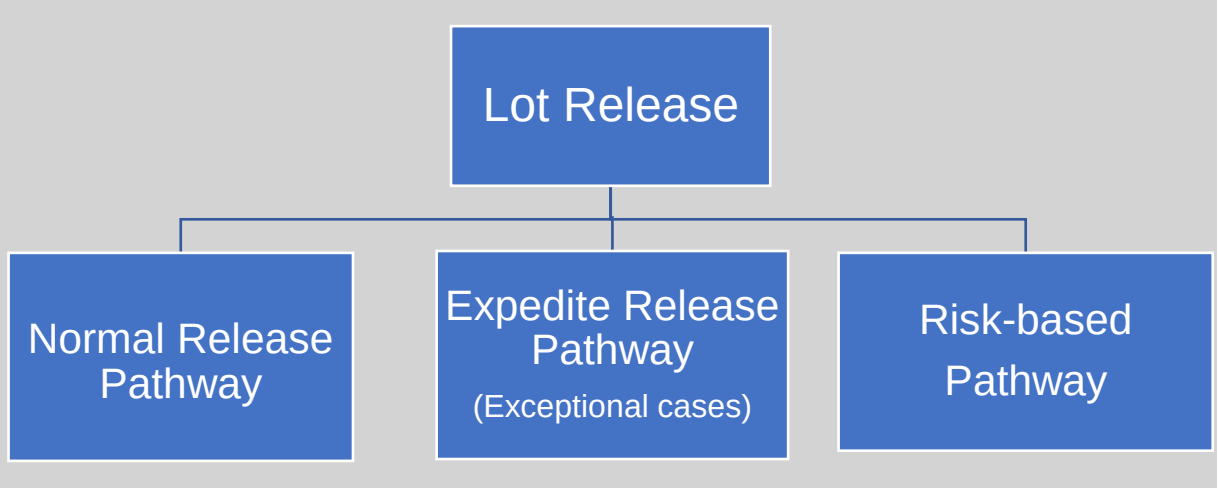
5.3.8 Maintenance of appropriate storage system; and

5.3.9 Assurance of data integrity.

NDCL follows WHO guidelines for national authorities on QA and other quality-related documents.

6. Conducting Lot Release

Figure 1. Lot Release Pathway



6.1 While Conducting Lot Release

6.1.1 The applicant should submit the relevant documents routinely with batches subjected to independent LR as per document checklist (Annexure of SOP No. NC-QA-GNL-056).

6.1.2 Documents to be submitted annually or when requested:

6.1.2.1 Annual Product Quality report;

6.1.2.2 Stability data;

6.1.2.3 Clinical trial documents;

6.1.2.4 Ethical approval document;

6.1.2.5 GMP certificates;

6.1.2.6 Annual Production Plan; and

6.1.2.7 Approved specification.

6.1.3 The manufacturers SLP is reviewed by NDCL/DGDA before release of a lot onto the market to ensure that specifications defined in the MA dossiers are met.

6.1.4 Where appropriate, review of the SLP could be complemented by independent Testing (partial/complete testing) as per Testing and Lot Release Procedure of Vaccines (NCL-QA-GNL-013).

6.1.5 Expedited LR may be performed based on the “reliance” mechanism in exceptional cases, including the following:

- Product shortage in Bangladesh;
- Public health emergency; and
- Biological product donated from international organizations.

Upon appropriate justification, LR may be considered based on the LRC provided by the country of origin's NRA and/or any other responsible NRA. This action will be considered only if the applicant holds a valid Emergency Use Authorization issued by DGDA.

Based on emergency/ outbreak of disease, the vaccine may be marketed or supplied without LR, subject to prior approval of the Licensing Authority (Drug and Cosmetics Act-2023). However, the LRC shall be obtained within the timeframe defined by NDCL/DGDA.

6.1.6 Product consistency will be assessed through trend analysis on successive lots (see section 7). When NDCL does not receive consecutive lots or receives only a small number of the production lots, interpretation of trend may require additional information (e.g., Annual Product Quality Report) from the manufacturer.

6.1.7 In case of imported vaccines, any available LRC issued by the responsible NRA/NCL, from the producing country, should be considered in the overall assessment of a vaccine lot. If the LRC is not provided with the summary protocol, the NDCL/DGDA have the authority to request it. Any further document pertaining to the related lots may also be requested by NDCL/DGDA if necessary.

6.1.8 The LR will be based on review of the SLP, testing result (manufacturer), and the LRC from the country of origin. However, in rare circumstances, a few vaccine LRCs may not be issued by the country of origin; in that case, NDCL, DGDA will do a LR based on CoC/CoA by country of origin.

6.1.9 Parallel testing may be performed where a quicker LR is required.

6.1.10 A risk-based approach for analysis (RA) will be applied while deciding a testing policy. To decide a risk-based approach consistency of the product will be evaluated as per procedure (NC-QA-GNL-013). Consistency will be assessed based on:

- Previous testing report in NDCL;
- Manufacturer's yearly test report;
- DGDA GMP inspection report; and
- Trend analysis data of NDCL and manufacturer.

Table 1. Risk Group categorization with requirements vs LR actions:

Risk group	Risk Rating	Requirements	LR Actions
1	**High risk**	• Newly registered vaccine including biological product (first 3 batches after registration). • Variation to the manufacturing process/method or already registered products. • Product that failed to achieve consistency in production and testing.	Document review Testing + testing of entire parameters (full testing).

Risk group	Risk Rating	Requirements	LR Actions
2	**Medium risk**	• Product that failed to achieve consistency in production and testing (5 years)	Document review Testing + testing of partial parameters (partial testing).
3	**Low Risk**	• Product has demonstrated batch consistency and good compliance (not less than 20 batches). • Every five batches for locally manufactured human vaccines, imported human vaccines, and other biological products with document review. • One batch to be analyzed for every five batches + summary protocol review.	Document review only and for locally produced human vaccine periodic testing and for imported human vaccine reliance mechanism should be applicable.

Based on the information, frequency and parameters of testing will be decided.

NDCL maintains appropriate laboratory facilities with experienced, competent, and skilled laboratory staff along with an established QMS for performing independent testing when required.

6.1.11 **The expected time frame for LR with or without testing:** Maximum time taken by NDCL for the analysis of samples and certification after receiving all the necessary and/ required relevant documents and or samples are as follows or as per SOP of NDCL/DGDA:

- **Products to be released on complete testing:** LR of the product depends on receipt of sample, SLP, and other relevant documents. The duration of LR will be counted from the day when samples, SLP, and documents are completed and submitted to NDCL; LR will be completed within 120 days of last submission.
- **Products to be released on partial testing:** All the products that will be subjected to partial testing (appearance, sterility, identification, and potency) will be released within 35 days after receiving all the necessary and/ required documents and/or samples. If the potency test is in-vivo testing, then the release period will be 90 days.
- **Products to be released on protocol scrutiny only:** The review of summary protocols is done by using relevant checklists. Stringent control on the documentation is applied. The product will be released within 21 days after receiving all the necessary and required documents. Any discrepancy, gaps, or deviations identified during protocol review shall be informed to the manufacturer and NRA (if necessary) for early resolution and in this case of discrepancy, gaps, or deviation. The LR time frame will be extended accumulating the required time for resolution.

6.2 Protocol Review

The format and content of the protocol is finalized and approved by the NDCL/DGDA during the review of the license application, and the format of the protocol will be amended in response to changes in the approved production process and approved by the NDCL, DGDA.

The manufacturers send the SLPs that contain summarized information taken from the production and test records according to GMP requirements to ensure that the lot meets the specifications in the MA. A manufacturer's SLP will be approved by the appropriate QA or QC responsible person and submitted to NDCL/DGDA.

6.2.1 Principles

Protocol review is conducted by the NDCL/DGDA lot release committee. The same format of the summary protocol will be used for the same product in different markets. In case the vaccines are to be exported outside of Bangladesh; the protocol format may be adjusted depending on the information required.

Independent review of critical data from each lot of vaccines is essential to:

6.2.1.1 Assure the quality consistency of every lot of each vaccine;

6.2.1.2 Obtain confidence in the strength of active components claimed; and

6.2.1.3 Assess the validity and accuracy of the tests performed.

NDCL/DGDA reviews the traceability of critical source materials, active and critical components used in the manufacture of the product, used reference standard/working standard, and the results from tests performed by the manufacturer at various stages of production, including tests performed on critical components, intermediates, final bulk, and final product.

However, lot release certificate will be issued based on careful review of the information on the final product.

6.2.2 Summary Protocol Template

The SLP format is approved by NDCL/DGDA. The format is developed as per WHO templates and the information and specific requirements from the approved MA dossier.

The summary protocol template is a controlled document. If there are any changes to the template due to changes in the manufacturing process or testing, they should be traceable and approved. The lot release committee is responsible for reviewing these documents and ensuring that the latest version of the license is reflected in the SLP submitted by the manufacturer.

Each SLP is vaccine specific, but a summary protocol should cover some general items (see Table 2).

Table 2. Information to include in the summary lot protocol for review:

Items	Essential Information to Cover	Critical Parameters to Review
Identity of manufacturer	• Name of the manufacturer	• License validity check, latest inspection report
License number	• Unique license number	• License number
Site(s) of manufacturing	• Site of manufacturing for each bulk, final bulk, and final product	• Name and address of each bulk, final bulk, and finished product manufacturing site.
Name of the product	• Trade name and International/common name	• Approved trade name and international/common name according to MA dossier.
Name and lot number	• Name and lot numbers of the final products, bulk, final bulk, and the diluent, if applicable	• Final lot name and lot number, each bulk lot number (if applicable), • Final bulk lot number and diluent lot number (if applicable).
Lot size	• Volume, number of doses and type of container	• Batch/lot volume, final production batch size, number of doses, container details.
Expiry dates	• For each starting material (if applicable), intermediates, final bulk, and final product.	• Expiry date of each starting material (if applicable), intermediates, final bulk, and final product.
Dates of manufacturing	• Each critical starting material (e.g., seed lots, cell banks, starting materials of animal origin etc.), intermediate, final bulk, and final product.	• Check and compare against noted expiry dates etc.; to calculate and confirm values.
Flow chart	• Flow chart for the traceability of manufacturing process for major components including lot numbers.	• Identity and logic flow for starting materials, intermediates, final bulk, and final product confirmed with room environmental details (wherever required).
Strains and cell substrates	• Name, seed lot number, passage number.	• Strain of production seed and type of cell substrate, lot/bank number, passage number of master and/or working lot/bank are the same as the one approved by DGDA on MA and/or recommended by WHO (e.g., oral polio vaccine).
Manufacturing process	• Each production process (such as cultivation, purification, inactivation), the methods of QC tests as well as their release specifications, and the results obtained. Lot number of intermediates and their size/volume, storage conditions.	• Confirm they are the same as per approved dossier by MA. • Confirm the yields of critical production processes are within the acceptable range.
Formulation	• Date of formulation. • Number of active components in the final formulations with the lot	• Date of formulation. • Verify calculated and actual values based on information provided as per product specific annex.

Items	Essential Information to Cover	Critical Parameters to Review
	numbers and volumes of bulk concentrates.	
Quality control tests	• Actual results of tests on critical starting materials, intermediates, final bulk, and final product and the specification. Include the individual tests and the mean value. • Testing method should be validated/verified. • Provide the starting date of test, method, and a list of reference preparations, standards, critical reagents and their qualification status, performance of relevant reference preparations, standards, and internal controls such as results of assay validity criteria (for example, slope, intercept, linearity, 50% end points, results of internal controls, challenge doses). • Provide with statistical results, such as, mean, geometric mean, standard deviation (SD), 95% confidence intervals, if applicable. Include results of failed tests or note invalid tests if a test has been repeated.	• Date of QC tests for identity, purity, safety, potency (strength), and ensure thermostability of the product are following the approved specifications. • Check traceability of validated/verified method, reference material, test parameters, and result.
Details on final lot	• Filling and sealing information, physical checking and labeling, packaging details.	• Check details of filling and sealing information, physical checking and labeling, packaging details with environmental condition of the room.
Storage condition of finished product	• Detail information of storage condition (temperature, humidity).	• Check data of storage condition.
Batch release certificate from manufacturer	• Name of the product with batch number and quantity; and • Method reference.	• Check the batch release certificate and method reference.

6.2.3 Checklist for Summary Lot Protocol Review

NDCL uses a vaccine-specific checklist in the review of SLPs to ensure a thorough review. A checklist for each section of the protocol should be developed to ensure a complete review of the information. Checklists have been developed according to the critical parameters in the production and control processes, such as strain and acceptable passage level of seed, acceptable passage level of cell substrate, purification method, methods and release specifications of QC tests, and shelf life of intermediates. Checklists are vaccine specific for a registered product and/or a test, in accordance with both the MA

dossier and WHO Technical Report Series (TRS) 978 (WHO Guidelines for Independent Lot Release of Vaccines by Regulatory Authorities Geneva, World Health Organization, 1992, Annex 2) and may be a copy of the protocol template with the specific required manufacturing information included for reference (e.g., name of the cell line, origin, testing methods and specifications for starting materials, intermediates, final bulk, and final product.)

6.2.4 Protocol Review Process

The SLP review process is highly dependent on the quality of the information provided by the manufacturer. Reviewing SLPs requires a good understanding of the product and laboratory control methods. After receiving the document from a manufacturer for LR of a product, documents are reviewed by the lot release committee and approved by NDCL/DGDA. A validated database (LIMS) with adequate access controls and traceability for trending and tracking of the data submitted is maintained by NDCL.

NDCL/DGDA starts the LR process with the receipt of manufacturers' documents, including packaging and labeling insert and required number of test samples. After initial verification of the label information for the test sample and on the SLP, the protocols are documented into a database or otherwise recorded. At receipt, the first step in protocol review should be confirmation that the manufacturer has used the approved template for the given vaccine. Then the protocols are routed to the lot release committee within the NDCL/DGDA that had already been formed based on their expertise. This should be traceable according to QA management procedures.

NDCL maintains databases for capturing information on, for example, lot size, results of tests, and information of reference standards and controls that are useful for tracking and trending of information for a particular test or section of the protocol. The results of tests and performance characteristics of reference standards and controls and specification limits including appropriate confidence intervals of typical results for a specific period will be shown. In all cases, databases will be secured to avoid unauthorized addition, revision, or deletion of information, and a backup system should be provided. A trend analysis SOP (NC- QA-GNL-031) has been developed for tracking and trending of manufacturers' results and information describing parameters to be tracked and trended, frequency of periodic reviews, and actions to be taken in case of out-of-trends, among others.

In general, a particular lot of the product is satisfactory if the protocol review shows that all the elements described in the Table in section 6.2.2 have been compared against the characteristics approved by competent authority and have been found to be compliant.

For freeze-dried/thawed vaccines, the protocol or CoA of the particular lot of diluents is also reviewed.

6.2.5 Handling Discrepancies and OOS Results in Summary Protocols

In the submitted SLP, any discrepancies, errors, or OOS found will be documented and verified before communicating them to the manufacturer. NDCL/DGDA developed a procedure to communicate this issue and related activities to the manufacturers or the vaccine-producing country's NRA to resolve issues with appropriate traceability. This may

include formal notification by memo or letter, an email, or minutes of telephone discussions. Manufacturers' responses should be reviewed and documented in making the decision on the lot. This can include the manufacturer's submission of the corrected page/version of the summary protocol, which then should be traced by NDCL/DGDA.

Depending on the type and extent of the mistakes or discrepancies, the manufacture may be required to investigate to ascertain the root cause of the errors or discrepancies, as well as procedures for corrective and preventive measures to avoid such issues in the future. For imported lots, communication with the producing/releasing country's NRA may be required. For producing/releasing countries, communication with the country inspectorate could be required. Such information exchange can help to judge the corrective and preventive actions introduced by the manufacturer.

6.2.6 Sampling

6.2.6.1 Sampling procedures should secure an adequate number of samples required for testing and storage. Those samples should also be representative of the batch/ commercial consignment for LR testing.

6.2.6.2 The samples collected should be a representation of the LR or commercial consignment.

6.2.6.3 If resampling is required for retesting, the NDCL will provide guidance on sampling location.

6.2.6.4 For locally manufactured lots, samples should be taken from each of the sampling points, that is, from the beginning, middle, and end of the filling run. Containers should be clearly labeled to distinguish them from the part of the filling run where the samples originate. The manufacturer will be informed by the NDCL/DGDA of any change/reduction in the sampling points subject to sufficient data confirming the consistency of production.

6.2.6.5 Samples should be transported and submitted at the appropriate temperatures to NDCL. Appropriate validated cold box with cold chain monitors (minimum Data Logger or Q tag) should accompany each batch of vaccine and other biologicals. The NDCL will receive samples during office hours (excluding government holidays, weekends). No sampling will be performed unless temperature monitoring devices ensure that excursion (cold chain breakage) of temperature, if any, is within the acceptable limit.

6.3 Independent Testing

NDCL developed technical expertise that enables independent testing to monitor and assess the key product QC parameters and consistency of product as well as other issues when they arise.

NDCL/DGDA has subcontracting procedures that allow for LR testing to be performed by a laboratory other than NDCL. Subcontracted laboratories are pre-assessed according to NDCL protocol. All information exchange will be handled in a confidential manner and

there will be a system to ensure that there is no conflict of interests. The final decision on the test results lies with the responsibility of NDCL/DGDA.

6.3.1 Purpose of Independent Testing

NDCL/DGDA has developed a LR testing program to verify manufacturers' test results. All testing is performed in a systematic way by qualified NDCL personnel and monitor the continuing suitability of the methods and reference materials and allow detection of possible unaccounted for drifts in these parameters. The LR program uses defined mechanisms that provide feedback for the MA department. The LR program complements the DGDA GMP inspectors to establish a holistic approach to vaccine QC.

6.3.2 NDCL, DGDA Independent Testing for Lot Release

A defined procedure, Testing and Lot Release Procedure for Vaccines (NC-QA-GNL-013), is established for testing as part of overall LR activities. NDCL staff are involved in the MA evaluation process (for pharmaceutical quality information at least) and should have knowledge of the MA dossier and be and able to identify and assess the critical parameters for testing.

The NDCL QMS supports the policies of the LR program. The NDCL has established a QMS that complies with ISO and is recognized as an International Organization for Standardization accredited and WHO-prequalified testing laboratory. Vaccine-specific test methods are validated following QA standards (including equipment qualification) before independent testing is performed. NDCL has established documented and approved procedures and guidelines both for internal use and for transparency with any partners, including other NDCLs and the product manufacturer.

NDCL has a good communication system with the manufacturer. NDCL will discuss with the manufacturer and MA department concerning the transfer of assays, if required, to allow transfer and qualification/validation of the methodology prior to applying to the first lot for LR testing.

Comparison of testing results between the NDCL and the manufacturer is important and done by trend analysis, since specifications for some biological assays (i.e., potency and or antigen content, identity, preservative content) are dependent on the analytical technique used to avoid potential discrepancies that may be related to the methodology used and not to the quality of the product.

6.3.3 Establishment of Testing Policy

NDCL implements LR testing policies by addressing the prerequisites noted in Testing and Lot Release Procedure for Vaccines (NC-QA-GNL-013).

To conduct independent testing, NDCL will estimate its own laboratory capacity and will take the information available from other NRAs/NCLs that can also release the same product.

The establishment of a testing policy should be made separately for each product and should consider four main aspects:

6.3.3.1 Should the vaccine be tested by an independent authority?

6.3.3.2 If testing is required, what critical parameters should be tested by the NDCL?

6.3.3.3 Should testing be done on every lot or on some reduced percentage of lots?

6.3.3.4 Are testing results available from another NCL?

The following points are considered that may influence the testing policy:

- Nature of the final product (live, inactivated);
- The biological nature and complexity of source material;
- The complexity, robustness, and level of control of the manufacturing process; and
- The nature and complexity of the QC methods.

Manufacturers' production history and other information required for deciding testing policy will be obtained from SLP and/or yearly vaccine and/or biologic product reports in some circumstances that contain production and testing information. Other information may be obtained from the GMP inspection report, adverse events following immunization report, product compliance, and other post-marketing surveillance safety and quality information. The testing policy for the same product at other NCLs may also be taken into consideration in establishment of the testing policy.

6.3.4 Criteria for Selection of Tests for Lot Release and Percentage of Lots to be Tested

Once the decision to perform independent testing is taken, the NDCL will concentrate on selection of critical elements from the MA requirements to be tested and the percentage of lots to be tested.

Key elements of focus where tests may be considered necessary include appearance, identity, potency, specific safety, and for some products thermostability (e.g., oral polio vaccine). Systematic testing of simple physical-chemical parameters may not be the highest priority when considering the best use of resources. Some parameters are better monitored through other tools, such as GMP compliance (e.g., sterility testing by aseptic process validation and environmental monitoring by the manufacturer). In all cases, the added value of the independent results for the tests chosen should be carefully considered in the context of the overall evaluation of the lot.

Testing is focused on the final product. The formulated final bulk may be tested in some cases (e.g., in the case of combination vaccines). Nevertheless, a complete evaluation of the properties under question may require assessment of upstream components

(e.g., monovalent bulks). This may also be necessary if test procedures cannot be applied to final products (e.g., if the presence of adjuvant in the final product prevents immunochemical analyses).

Specific attention will be paid to new vaccines, new manufacturers that have little accumulated experience, and sophisticated combined vaccines for which testing and interpretation of results can be complicated.

DGDA approves the developed and adopted testing method. If a different test method is used by the NDCL, for example, in case of discrepant data between the manufacturer and the NDCL, then the approved test method defined in MA should be used to solve the test issue.

There will be a regular review of the testing policy to reevaluate needs and appropriateness in the current situation. Additional tests may be included, or existing tests deleted, as required. Informal testing outside of a planned program without sufficient preparation should be avoided, as this can generate nonrelevant or misleading test results.

The percentage of a given product's lots to be covered by the testing program will be described in the internal procedure in advance. If a reduced percentage of lots is tested, the lots should be representative of the total production (e.g., selected number of bulks covering a maximum of final lots or selection of filled lots issued from the same bulk). If fewer than 100 percent of lots are tested, the decision on which lot will be tested will be controlled by NDCL, and the manufacturer will not be aware of it.

The percentage of lots tested should be monitored and revised, if necessary, based on the experience with the product and data from the yearly biological product report. For example, good consistency over a significant period may lead to reducing the percentage of lots covered, while observance of an undue number of failing results and/or specific testing issues may result in an increased percentage of lots to be tested.

Development of testing methodology and capability should begin as soon as possible for both NDCL/DGDA and manufacturer, possibly at the clinical trial stage. However, while testing of samples by an NCL for clinical trial approval stage is recommended in WHO guidelines, this is not considered LR *per se*. Although additional guidance in this area is needed, this document focuses only on the LR procedure for licensed products.

6.3.5 Importance of Reference Preparations for Lot Release

Appropriate use of reference preparations in independent testing is of critical importance for the interpretation of the results. This has a particular impact on the ability to make relevant comparisons between test results from different laboratories (e.g., manufacturer and NDCL) and the decision-making process.

Control charts of critical parameters in reference preparations should be kept and continue to monitor performance over time. This allows an overview of both the reference preparation activity and the method. For example, it could show if there has been a trend or a shift in the reference standard attributes, such as slope, intercept,

and 50 percent endpoint that may indicate problems with stability of the reference standard or changes in other assay systems, for example, animals, cells, and critical reagents. Another example of the utility of trend analysis is the assay validity criteria based on 95 percent confidence intervals. If the assay validity criteria on any attribute of the reference standard, slope, intercept, or potency of control is based on 95 percent confidence intervals and the actual data do not show approximately 95 percent acceptance of the assay based on that attribute, there may be problems with setting the limits or performance of that attribute.

The observations from this exercise can be important for feedback to MA authorities and/or bodies involved in biological standardization activities and can be used also to evaluate the appropriateness of the reference materials used and/or the need for new ones.

Reference reagents are developed to improve standardization of assays. They are becoming increasingly important in the context of new vaccines such as multi-component vaccines. In many cases, the reference reagents are established and prepared by the manufacturer, as they are often product specific. These reference reagents should be calibrated in International Unit against an IS when it exists.

6.3.6 Standards

NDCL will procure working standards and reference standards/secondary standards for test and/or analysis of vaccines and biologicals. Until NDCL can procure a working standard, it will use the WHO IS as a basis for the calibration of secondary standards.

6.3.7 Practical Considerations

The number of final lot or upstream components samples in a given product requested by NDCL should be appropriate for the testing required, and the sampling procedures will ensure the representativeness of the lot in question. A system will be in place for recording, tracking, and appropriate storage of all samples upon receipt from the manufacturer.

It may be necessary to obtain product-specific reference materials or reagents from the manufacturer. The amount requested should be relevant to the amount of testing to be performed and not place undue stress on the supply of the material, as it is often available in limited stocks.

The time required for testing is an important issue, as it can greatly influence the supply chain and can have a significant impact when products have short shelf lives. This can be of particular concern when in vivo tests, which can take several weeks to complete, are involved. Under certain circumstances, the NDCL/DGDA may agree to receive samples from manufacturers before they have completed their own test procedures so that testing by the NDCL is done in parallel. In such cases, the lot cannot be released by the NDCL until all the test results from the manufacturer have been received (including the completed and signed final summary protocol with their test results). The

NDCL will evaluate the risk benefit of parallel testing, mainly considering the frequency of lots rejected by either the manufacturer or the NDCL.

When animals are used for testing, the NDCL should be aware of the potential variability of the source, housing, and handling of animals. NDCL will apply the reduction, replacement, and refinement principles to minimize the use of animals for ethical reasons. Validated in-vitro alternatives should be favored wherever possible. However, the type of testing should be driven by the scientific need for valid relevant data. Moreover, agreements will be sought with NDCL from the exporting country or other NDCLs in a mutual recognition or collaborative agreement to utilize results of animal testing already performed by another NDCL in the spirit of minimizing animal testing worldwide.

6.3.8 Release Specifications

NRA LR function will pertain only to products that have a valid MA in which specifications have been approved by DGDA. Usually, NDCL experts are involved in assessing test methods, validity criteria, and product specification prior to MA approval. There is also a procedure to inform NDCL of any variations of the approved license specifications.

6.3.9 Result Processing by Using LIMS

LIMS is an automated system for the entry, storage, distribution, report, analysis, and management of testing results, LR-related information, and other information available in the laboratory. The NDCL is using LIMS for handling the NRA LR process. When any manufacturer or importer who intends to obtain an LR approval applies to NDCL through DGDA via either a direct personal visit or an NDCL website visit. The NRA LR process will take place through a series of several procedures or steps, including SLP review, QC testing, entry of testing log and results, confirmation of testing results, approval, and date of issuing LRC.

6.3.10 Evaluation of NDCL Results

The NDCL test results should be assessed against the specifications approved in the dossier. It is understood that the variability expected in the results for a given test method for a given product should already be accounted for in the specifications. To be in compliance with the MA, the test result should fall within the defined acceptance criteria, which are based on the validated methodology used by the NDCL and the specifications approved in the MA.

The NDCL will define and follow its own retest policy, if applicable. A combination of their results will be performed and include how these results are evaluated. The acceptance criteria should also be predefined and laid down in relevant SOPs.

The NDCL has a predefined standard procedure to deal with results that do not comply with the specifications. This procedure includes confirmation that the results reflect the actual quality of the lot tested and is not due to analytical error by the NDCL or the influence of variables unrelated to the product.

The manufacturer will be notified when an OOS result is confirmed, and exchanges should ensue to try to identify the cause of the discrepancy.

A test report, including the results and outcome of all the testing, will be prepared for the final evaluation of the lot and the decision-making process.

7. Data Monitoring

All critical quantitative data from QC results and especially potency from the manufacturer or other sources NDCL will be used for trend analysis as an essential part of LR. Statistical analysis will be conducted once sufficient data have been accumulated. The alert or warning limits and action limits of consistency trends will be defined on statistical grounds. Generally, ± 2SD and ± 3SD of the mean are set for the alert or warning limits and action limits, respectively, when data are normally distributed. In general, the variability and precision of the test will be considered when defining the limits. Care will be taken in interpreting such limits when based on small data sets. Trend analysis of key parameters may be requested from manufacturers or the responsible NRA/NCL. More complex specific trend analysis statistical methods can be used when sufficient data and expertise are available, particularly when data are not normally distributed. In addition, a set of data from a certain period (e.g., six months or one year) will be analyzed statistically compared to that of the previous period to detect any significant differences or shifts in trends.

NDCL has an established procedure describing this tracking and trending of manufacturers and, where available, the NDCL results will be developed. This procedure "Trend Analysis of Vaccines" (NC-QA-GNL-031) will describe parameters to be tracked and trended, frequency of periodic reviews, criteria for judgment, and actions to be taken in case of out of trends, among others.

7.1 Trend Analysis Including the Data from the NDCL

NDCL will perform independent testing of lots. All data from the tests, including the performance of reference standards and controls, will also be trended, and analyzed. It should be kept in mind that not all countries test all consecutive lots from a manufacturer. For these cases, the interpretation of trends will be made with caution and may require additional information from the manufacturer either directly or through contact with the relevant national inspectorate.

7.2 Comparison of Results of the Manufacturer with those of the NDCL

Results from the NDCL will be compared with those of the manufacturer. Any systematic differences will be documented. Any differences in trends will be investigated and resolved in collaboration with the manufacturer. Testing by the NDCL may, however, occur months after the manufacturers' release, so this should be taken into consideration when the NDCL makes the comparison.

8. Cold Chain Management and Monitoring

Vaccines and other biologicals are very sensitive to temperature; that is why it is very important to comply with the approved storage methods and conditions in the process of manufacturing, distribution, storage, and end-user use. If the temperature shows any deviation at any steps mentioned above, it will adversely affect the safety, efficacy, and stability of vaccines and other temperature-controlled biologics. In the case of an imported human vaccine, a vaccine arrival report should be submitted to the NDCL for each lot and shipment to be released.

Where a lot is imported in multiple shipments, each shipment's documentation should be clearly distinguished. The document should include the following information:

8.1 Invoice of product.

8.2 The product name and lot number clearly visible on all documents.

8.3 The date, time, and location of dispatch and receipt of shipment.

8.4 A copy of the air way bill.

8.5 The quantity per shipment.

8.6 A packing list indicating the number of containers/shipments and the number of per container/shipment doses.

8.7 A temperature monitor check sheet indicating the number of temperature devices per container/shipment, serial number, location (for example, inside top or bottom or outside the container), and status of each temperature monitor (a temperature excursion noted or whether it malfunctioned). Freeze tag information should be provided in instances where vaccines are not allowed to freeze.

8.8 The vaccine lot number and the number of the container/shipment should be clearly indicated on the document displaying the temperature monitor data. Alternatively, supporting documentation should be attached showing the serial numbers of electronic monitors used in each container of the shipment.

8.9 Raw data from electronic temperature monitoring devices (including Q Tag WHO Type 1 monitors) is required, except for devices where a summary is automatically generated. In these cases, the summary is preferred.

9. Evaluation of the Lot and Decision-Making Process

9.1 Establishment of Decision-Making Procedures

The head of NDCL is responsible for signing the LRC. Once all respective lot documents are available for final evaluation, a formal decision-making process is in place to decide whether the given lot can be released. An established procedure is in place to clearly describe the LR process and required documents for the final decision [Testing and Lot Release Procedure for Vaccines (NC-QA-GNL-013)]. Good coordination and communication are needed, especially to address when different bodies, such as NDCL/DGDA and manufacturers and importers, are involved in this process.

To provide continuity and develop expertise on each product, it is desirable that product specialists be assigned with the responsibility of managing the relevant information for each product. A general LR process chart is in place outlining the lot approval process and the person responsible for each activity.

The approach to independent LR by the lot release committee will be appropriately described in NDCL LR flow charts. Procedures will cover the relevant options used: release upon review of summary protocol only and/or release upon review of summary protocol plus independent testing (partial/full testing) by NDCL. The respective flow chart defines the initial step of receiving an application through when the final decision is taken based on the formal written conclusions. SOPs or documents are necessary to cover the following essential elements:

9.1.1 An SOP for summary protocol review describing all reviewing steps up to and including the conclusion on the summary protocol (e.g., need for manufactures' correction, review of corrected pages, investigation, conclusion).

9.1.2 The NDCL/DGDA has established a formal vaccine specific checklist regarding the summary protocol review, and this checklist will be filled out to ensure compliance with approved specifications and be signed by the responsible person.

9.1.3 An SOP is available for describing acceptance criteria for each parameter of individual vaccine as per the MA dossier and recording all the individual test results in a CoA.

9.1.4 After analysis of the vaccine by NDCL, a formal report will be developed by a responsible analyst to capture the test results, and the final CoA will be signed by the responsible person.

9.1.5 Results from testing and document review performed by NDCL are compared to the specification in the product MA file and all approved variations. If the results are found to be satisfactory, an LRC will be issued for each lot verified (see Annex 1 for Flow Chart for Lot Release of Locally Manufactured Vaccine and Annex 2 Flow Chart for Lot Release of Imported Vaccines).

9.1.6 If a vaccine lot conforms with the release requirements, NDCL will notify the relevant department via paper file or electronically and provide a hard copy of the LRC.

9.1.7 If a vaccine lot does not conform to the release requirements due to an OOS test result, and after investigation a quality defect is confirmed, NDCL will issue a noncompliance certificate to the manufacturer and inform the DGDA MA department. The MA department will take regulatory action by issuing a letter to the manufacturer mandating destruction of the mentioned OOS product. The manufacturer will destroy the OOS product in the presence of a local NRA authority. The manufacturer will provide a certificate of destruction or relevant destruction document to the DGDA MA department and submit a copy to NDCL.

9.1.8 In a case where there is evidence that the cold chain of a shipment or part of a shipment was not adequately maintained or controlled, the affected doses will

not be released. The MA holder will be instructed to destroy the affected doses as stated in 9.1.7.

9.1.9 A retest policy developed to follow general QA principles defines the policy for retesting and handling of OOS results. In addition, an SOP is in place to give guidance on the retesting policy according to product-specific recommendations (e.g., combination of results and calculation method). If any noncompliance occurs, a full traceability investigation will be conducted on test reports, and the manufacturer will be contacted for further investigation and record the communication. As part of QA, in the event of derogation, an SOP exists to outline the decision-making process including documentation and written criteria to support the decision made.

9.1.10 An SOP describes the acceptance criteria for vaccines LR in exceptional cases when deviation from the normal procedure is necessary. Examples include release for an emergency or crisis, urgent need due to a critical supply shortage, when information is pending regarding correction for summary protocol, or in the event of discrepancies between NDCL and manufacturer's test results. The procedure will be developed based on a risk/benefit analysis, considering all available information. This will be applied only by the head of NDCL for signing the release certificate with approval from the DGDA. Documentation supporting compliance with approved specifications (summary protocol review and test reports, if applicable), will be included.

9.1.11 All the steps in the decision-making process will be documented.

9.2 Reliance of/Confidence in Lot Release by Other NRAs/NCLs

In cases where a lot has already been released by another NRA/NCL, it may be possible to accept that lot for release based on the existing release certificate. NDCL/DGDA has a mechanism for reliance of test result and LR by another NRA. NDCL has a list of NRAs/NCLs that it recognizes. NDCL maintains strong collaboration and communication between the different NRAs and a good level of transparency (Section 73, Drug and Cosmetics Act-2023).

Agreements covering specific products enable NDCL/DGDA to accept the test results provided by another NRA, thus avoiding repeat testing and facilitating harmonization without compromising the safety and quality of the product or extending the agreement to full mutual reliance of all LRs. The test results provided by another NCL could thus be used, in addition to the protocol evaluation by NDCL/DGDA, when they evaluate the lot for release.

These types of approaches provide the advantage of limiting repeated evaluation and testing, and they serve to streamline the release procedure. Other benefits of the confidence building required for such approaches may be training and capacity building for review and product assessment. NDCL will always ensure the integrity and confidentiality of the stakeholders, including manufacturers and procuring agencies.

9.3 Release Certificate Issued by the NRA/NCL of Producing/ Releasing Country for UN Procurement

NDCL will release vaccines supplied through UN agencies without testing because such products are prequalified by WHO. The release certificate issued by the responsible NRA/NCL should be forwarded by the UN agencies to the receiving country's NDCL, DGDA and the summary protocol will be provided upon request. NDCL/DGDA may consider review of the SLP and/or testing to develop competency and confidence in their activity, as well as provide an overview of the vaccine's quality. However, if any deficient result is detected, the responsible NRA/NCL of the producing country should be consulted.

9.3.1 Product Labeling Information Review

NDCL also reviews the printed materials that accompany the vaccine batch to ensure that all labeling items comply with NRA's Drug and Related Product Labelling Regulations.

10. Fees Associated with Lot Release

DGDA plans to introduce fee for Lot Release in future. Once introduced, following procedure will be applied:

- Each application for the release of vaccine lot will be charged.
- Once an application has been filed and payment has been confirmed, there will be NO REFUNDS of the payment made.
- Applications that do not include the correct fees will not be processed.
- The applicant must provide the required fees in accordance with government approval.
- Any other Government procedures if applicable.

11. Lot Release Certificate

A release certificate for each vaccine lot will be issued by the NDCL, DGDA and sent to the manufacturer (and procuring agencies, distributors, local agents, or organizations, where applicable) confirming that the lot meets the approved specifications and related provisions. This release certificate is the official document that authorizes the manufacturer (and procuring agencies, distributors, local agents, or organizations, where applicable) to release the specific lot onto the market. The certificate will include the following information, but not be limited to:

11.1 Name and address of manufacturer;

11.2 Site(s) of manufacturing;

11.3 Trade name and common name of product;

11.4 Marketing authorization number;

11.5 Lot number(s) (including sub-lot numbers, packaging lot numbers, if necessary);

11.6 Type of container;

11.7 Number of doses per container;

11.8 Number of containers/lot size;

11.9 Start date of period of validity (e.g., manufacturing date) and/or expiry date;

11.10 Storage condition;

11.11 Presentation of packaging mode;

11.12 Signature and function of the authorized person and authorized agent to issue the certificate;

11.13 Date of issue of certificate; and

11.14 Certificate number;

Other details, such as dosage form, strength of the product, registration code (DGDA), issue number for lot release, may also be included in the certificate according to the requirements of different countries.

The conclusion is included clearly in the certificate, for example: “the lot mentioned above complies with the relevant specification in the MA and provisions for the release of biological products and has been approved for release.” The statement should also give an indication of what the release decision is based on, for example, evaluation of summary protocol, independent laboratory testing, and specific procedures laid down in defined document, as appropriate.

For those lots failing to comply with the provisions, a different certificate of non-compliance will be issued that clearly states that the lot is non-compliant, ideally with a different color from the approval certificate.

The LRC is in English.

12. Annexes

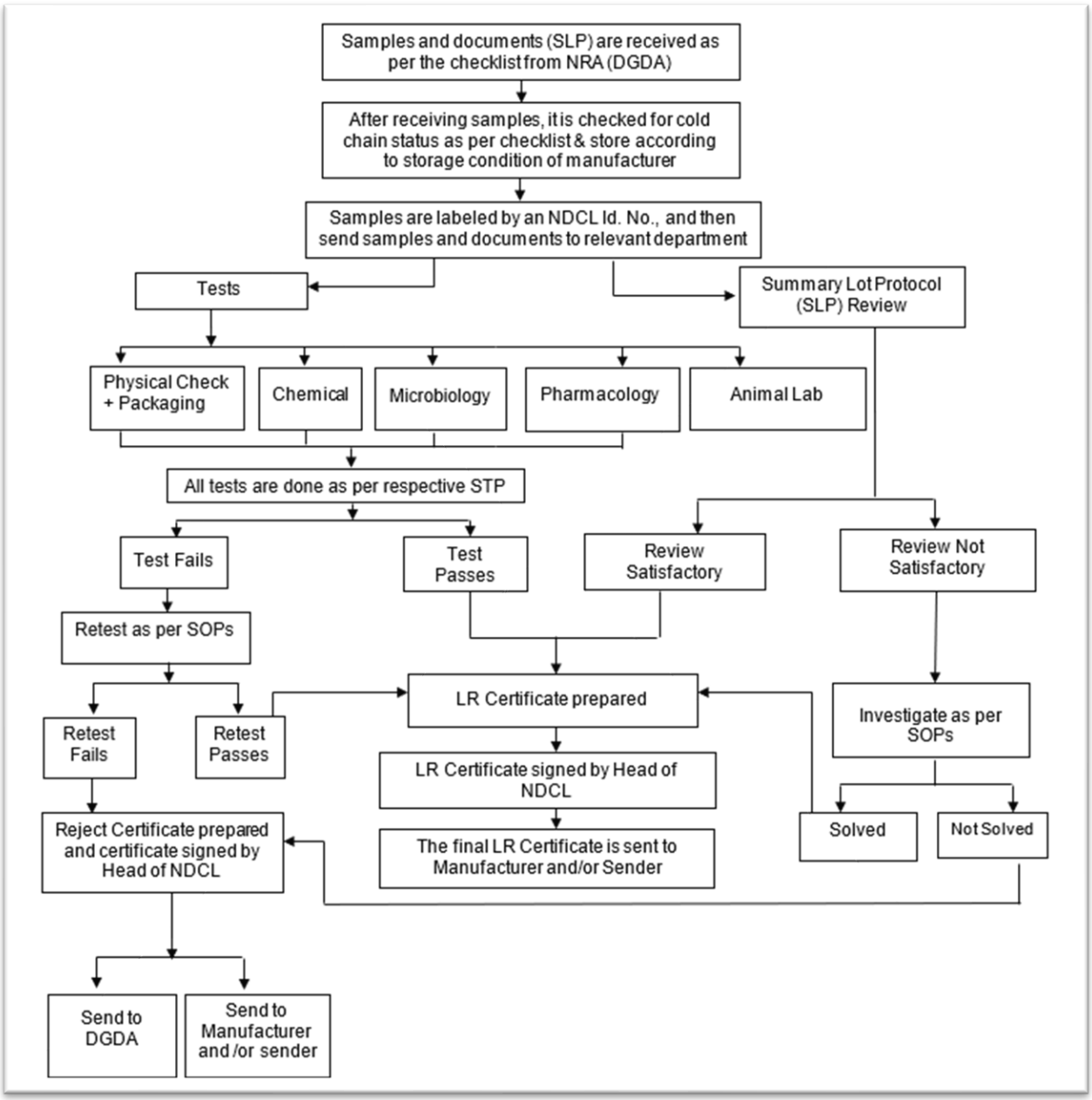
Annex 1: Flow Chart for Lot Release of Locally Manufactured Vaccines;

Annex 2: Flow Chart for Lot Release of Imported Vaccines;

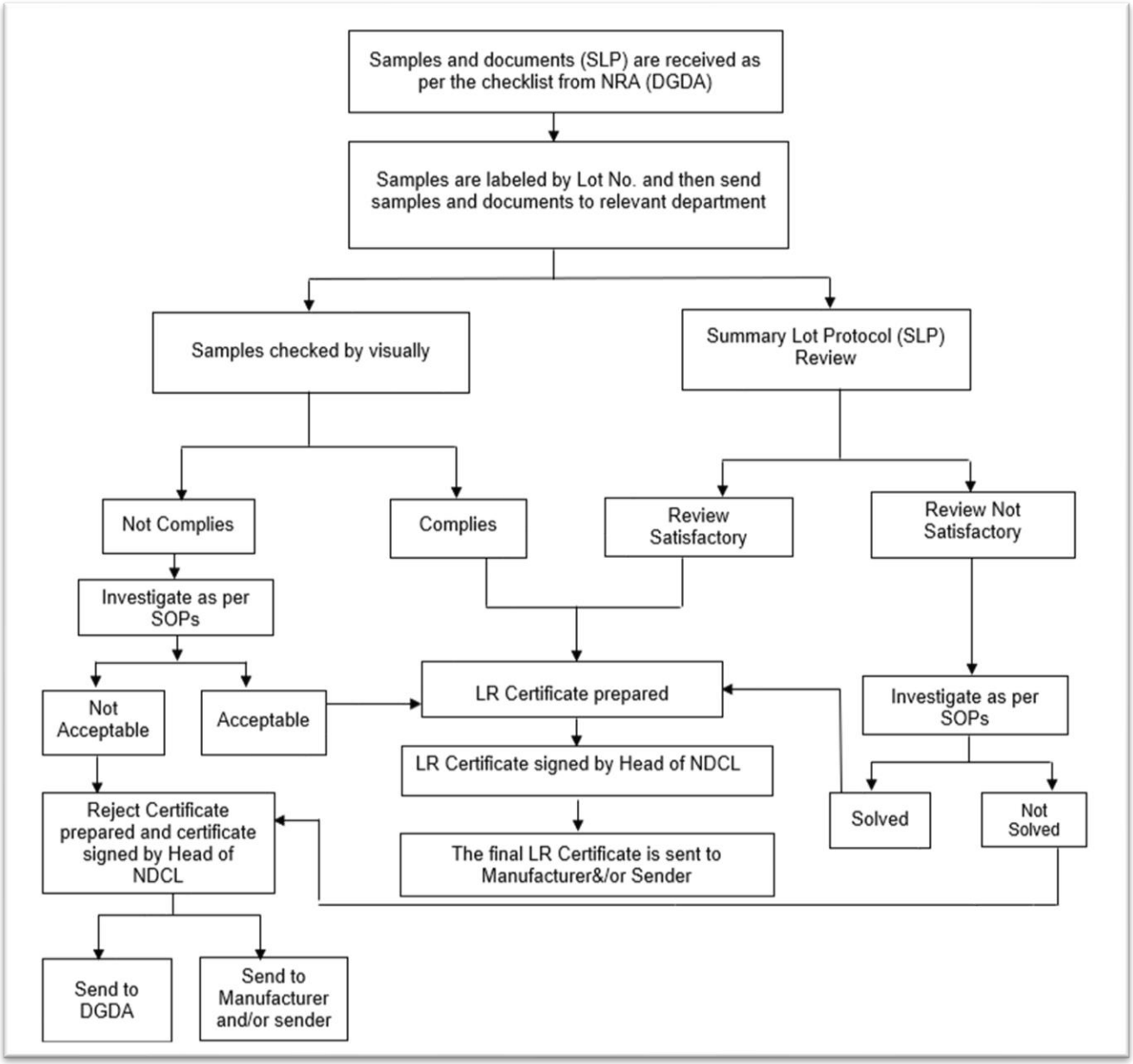
Annex 3: Drug and Cosmetics Act-2023 (Translation); and

Annex 4: Gazette Notification by Ministry of Health and Family Welfare (MOH&FW) (Translation).

Annex 1: Flow Chart for Lot Release of Locally Manufactured Vaccine



Annex 2: Flow Chart for Lot Release of Imported Vaccine



Annex 3: Drug and Cosmetics Act-2023

৬৭। **ভ্যাকসিনের লট রিলিজ।**—(১) লাইসেন্সিং কর্তৃপক্ষের নিকট হইতে দেশে উৎপাদিত এবং আমদানিকৃত সকল হিউম্যান ভ্যাকসিনের লট রিলিজ সনদ গ্রহণ করিতে হইবে;

তবে শর্ত থাকে যে, বিশ্ব স্বাস্থ্য সংস্থা কর্তৃক প্রি কোয়ালিফাইড এবং জাতিসংঘের কোনো সংস্থার মাধ্যমে সরবরাহকৃত ভ্যাকসিনের উৎপাদনকারী দেশের লট বিমুক্তকরণ সনদের ভিত্তিতে সংশ্লিষ্ট লট রিলিজ করা যাইবে।

(২) জনস্বাস্থ্যের জরুরি প্রয়োজনে অথবা দুর্যোগ বা আকস্মিক বিপর্যয়কালীন পরিস্থিতির গুরুত্ব, সময়ের স্বল্পতা এবং ব্যবহারের জরুরি আবশ্যকতা বিবেচনা করিয়া, লাইসেন্সিং কর্তৃপক্ষের পূর্বানুমোদন সাপেক্ষে, লট রিলিজ ব্যতিরেকে, কোনো নির্দিষ্ট ভ্যাকসিন বাজারজাত বা সরবরাহ করা যাইবে;

তবে শর্ত থাকে যে, পরবর্তীতে লাইসেন্সিং কর্তৃপক্ষের নিকট হইতে লট রিলিজ সনদ গ্রহণ করিতে হইবে।

(৩) গবেষণা অথবা ব্যক্তিগত ব্যবহারের জন্য স্বল্প পরিমাণ ভ্যাকসিন আমাদানির ক্ষেত্রে লট রিলিজ সনদের পরিবর্তে লাইসেন্সিং কর্তৃপক্ষের নিকট হইতে অনাপত্তি সনদ গ্রহণ করা যাইবে।

৭৩। **বিশ্ব স্বাস্থ্য সংস্থার তালিকাভুক্ত কর্তৃপক্ষের সিদ্ধান্ত অনুসরণ।**—অধিদপ্তর, প্রয়োজনে, তৎকর্তৃক গৃহীতব্য সিদ্ধান্তের ক্ষেত্রে বিশ্ব স্বাস্থ্য সংস্থার তালিকাভুক্ত কর্তৃপক্ষের সিদ্ধান্ত অনুসরণ করিতে পারিবে।

Section 67. Lot Release of Vaccines:

(1) Lot Release Certificate to be obtained from the Licensing Authority for Domestic as well as imported human vaccines.

However, Lot Release of WHO Prequalified Vaccines procured through any UN Organization may be done based on the Lot Release Certificate from the Country of Origin.

(2) In Pubic Health Emergency or disaster or acute emergency situation, considering the importance of the situation, time constraint and emergency of use, a vaccine could be marketed/distributed without Lot Release if prior approval from the Licensing Authority exist.

However, Lot Release Certificate must be obtained from the Licensing Authority afterwards.

(3) "No Objection Certificate (NOC)" can be obtained from the National Regulatory Authority (NRA) instead of Lot Release Certificate for importing small amount of Vaccines to be used for research or personal use.

Section 73. Adhering to the decision(s) of the World Health Organization (WHO) listed authority:

The Directorate, in case of any decisions to be taken by it, may follow decision(s) of the World Health Organization (WHO) listed authority.

Annex 4: Gazette Notification by Ministry of Health and Family Welfare (MOH&FW)

রেজিস্টার্ড নং ডি এ-১ "জাতির পিতা বঙ্গবন্ধু শেখ মুজিবুর রহমানের জন্মশতবার্ষিকী উদ্‌যাপন সফল হোক"

বাংলাদেশ গেজেট

অতিরিক্ত সংখ্যা
কর্তৃপক্ষ কর্তৃক প্রকাশিত

সোমবার, জুন ২৮, ২০২১

গণপ্রজাতন্ত্রী বাংলাদেশ সরকার
স্বাস্থ্য ও পরিবার কল্যাণ মন্ত্রণালয়
স্বাস্থ্য সেবা বিভাগ
ঔষধ প্রশাসন-১ শাখা

নং ৪৫.০০.০০০০.১৮২.২২.০০১.২১.১০৩ তারিখ : ২১ বৈশাখ ১৪২৮/০৪ মে ২০২১

পরিপত্র

বিষয়: **WHA (World Health Assembly) Resolution A67/32 অনুসারে ঔষধ প্রশাসন অধিদপ্তরের Pre-qualification অর্জনের নিমিত্তে Pharmacovigilance, Clinical Trial এবং Lot Release Indicator এর কার্যাদি সুচারুভাবে সম্পন্ন করার লক্ষ্যে এ সংক্রান্ত Function এর অনুমোদন।**

WHA (World Health Assembly) Resolution A67/32 অনুসারে ঔষধ প্রশাসন অধিদপ্তরের Pre-qualification অর্জনের নিমিত্তে Pharmacovigilance, Clinical Trial এবং Lot Release Indicator এর কার্যাদি সুচারুভাবে সম্পন্ন করার লক্ষ্যে নিম্নবর্ণিত নির্দেশনা প্রণয়ন করা হলো:

(a) Pharmacovigilance:

(১) মহাপরিচালক ফার্মাকোভিজিল্যান্সের কার্যকর সিস্টেম সুনির্দিষ্ট করিবেন এবং তদুদ্দেশ্যে, কেন্দ্রীয়ভাবে অথবা আঞ্চলিকভাবে, মানুষ অথবা প্রাণিদেহে কোন ঔষধের বিরূপ প্রতিক্রিয়া পর্যবেক্ষণের জন্য এক অথবা একাধিক ঔষধ বিষয়ক বিরূপ প্রতিক্রিয়া পরিবীক্ষণ সেল [Adverse Drug Reaction Monitoring Cell (ADRMC)] গঠন করিবেন;

(২) ঔষধ প্রশাসন অধিদপ্তর জাতীয় ফার্মাকোভিজিল্যান্স গাইড লাইন অনুসরণ করিয়া ফার্মাকোভিজিল্যান্স-এর সকল প্রয়োজনীয় কার্যক্রম পরিচালনা করিবে এবং সংশ্লিষ্ট স্ট্যাকহোল্ডার (stakeholder) উক্ত গাইডলাইন অনুসরণ করিয়া ফার্মাকোভিজিল্যান্স কার্যক্রম পরিচালনা করিবে;

(৩) ঔষধ, ভ্যাকসিন ও মেডিক্যাল ডিভাইসের আমদানিকারক অথবা উৎপাদনকারীকে তাদের প্রতিষ্ঠানের নিবন্ধিত পদসমূহের Safety Data এবং অনুমিত বিরূপ প্রতিক্রিয়া (Suspected Adverse Drug Event) সম্পর্কে লাইসেন্সিং কর্তৃপক্ষ বরাবর নিয়মিত প্রতিবেদন ও তথ্য উপাত্ত প্রেরণ করিতে হইবে;

(৪) সকল ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস উৎপাদনকারী, আমদানিকারী ও বাজারজাতকারী প্রতিষ্ঠান আবশ্যিকভাবে টিম গঠন করিয়া ফার্মাকোভিজিল্যান্স কার্যক্রম পরিচালনা করিবে এবং এতদুদ্দেশ্যে প্রতিষ্ঠানসমূহকে Focal Point সহ উপযুক্ত কোয়ালিফাইড পার্সন নিয়োগ করিতে হইবে;

(৫) লাইসেন্সিং কর্তৃপক্ষ প্রয়োজনে ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস উৎপাদনকারী অথবা আমদানিকারী অথবা বাজারজাতকারী প্রতিষ্ঠানকে বিশেষ অবস্থায় যে কোন ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস এর Safety অথবা Efficacy-এর উপর সুনির্দিষ্ট Study (Phase IV) পরিচালনা করিয়া প্রতিবেদন পেশ করিবার নির্দেশ প্রদান করিতে পারিবে। উক্ত নির্দেশ অনুসারে প্রতিষ্ঠানসমূহ প্রতিবেদন পেশ করিতে বাধ্য থাকিবে;

(৬) ঔষধ প্রশাসন অধিদপ্তর সকল ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস উৎপাদনকারী, আমদানিকারী ও বাজারজাতকারী প্রতিষ্ঠানে Good Pharmacovigilance Practice (GVP) অনুযায়ী পরিদর্শন কার্যক্রম পরিচালনা করিবে এবং ঔষধ প্রশাসন অধিদপ্তর ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস এর বিরূপ প্রতিক্রিয়া সংক্রান্ত রিপোর্ট Marketing Authorization Holder (MAH)/ঔষধ প্রশাসন অধিদপ্তর বরাবর প্রেরণের জন্য স্ট্যাকহোল্ডারদের মাঝে উৎসাহমূলক কার্যক্রম গ্রহণ করিবে;

(৭) বিভিন্ন আন্তর্জাতিক প্রতিষ্ঠান যেমন, World Heath Organization (WHO), United States Food and Drug Administration (USFDA), United Kingdom Medicines and Healthcare Products Regulatory Agency (UKMHRA), Therapeutic Goods Administration (TGA) Australia, Health Canada, European Medicines Agency (EMA) এবং অনুরূপ আন্তর্জাতিক মানের সংস্থা/ঔষধ নিয়ন্ত্রণ কর্তৃপক্ষ কর্তৃক ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস এর Safety সংক্রান্ত বিষয়ে জারীকৃত আদেশ/অ্যালার্ট/সিগনাল অনুযায়ী ঔষধ প্রশাসন অধিদপ্তর ব্যবস্থা গ্রহণ করিবে। প্রয়োজনে ঘোষিত ক্ষতিকর ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস ঔষধ নিয়ন্ত্রণ কমিটি (Drug Control Committee) কর্তৃক মূল্যায়নপূর্বক রেজিস্ট্রেশন বাতিল করা যাইবে; এবং

(৮) যদি কোন ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস উৎপাদনকারী, আমদানিকারী ও বাজারজাতকারী প্রতিষ্ঠান লাইসেন্সিং কর্তৃপক্ষের নির্দেশনা অনুসারে ফার্মাকোভিজিল্যান্স বিষয়ক কার্যক্রম পরিচালনা না করে অথবা করিতে ব্যর্থ হয়, তাহা হইলে লাইসেন্সিং কর্তৃপক্ষ প্রতিষ্ঠানের লাইসেন্স অথবা ঔষধ, ভ্যাকসিন ও মেডিকেল ডিভাইস এর রেজিস্ট্রেশন/মার্কেটিং অথোরাইজেশন সাময়িক বাতিল/বাতিল করিতে পারিবে।

(b) Clinical Trial Oversight:

(১) দেশে কোন প্রকার হেলথ কেয়ার প্রডাক্টের উপর ক্লিনিক্যাল ট্রায়াল অথবা Bio-equivalence (BE) study অথবা ক্লিনিক্যাল ট্রায়াল সেন্টার অথবা Contract Research Organization (CRO) পরিচালনার জন্য লাইসেন্সিং কর্তৃপক্ষ-এর অনুমোদন গ্রহণ করিতে হইবে। হেলথ কেয়ার প্রডাক্টের Clinical Trial অথবা Research অথবা Bio-equivalence (BE) study সরকার কর্তৃক অনুমোদিত Good Clinical Practice (GCP) গাইডলাইন অথবা স্বীকৃত আন্তর্জাতিক মানসম্পন্ন সংস্থা অথবা বিশ্ব স্বাস্থ্য সংস্থা কর্তৃক প্রকাশিত নির্দেশাবলি অনুযায়ী পরিচালনা করিতে হইবে। Clinical Trial অথবা Research অথবা Bio-equivalence (BE) study লাইসেন্সিং কর্তৃপক্ষ পর্যবেক্ষণ/পরিদর্শন করিবে;

(২) ক্লিনিক্যাল ট্রায়াল প্রটোকল (Clinical Trial Protocol) ঔষধ প্রশাসন অধিদপ্তর/লাইসেন্সিং কর্তৃপক্ষ কর্তৃক অনুমোদিত হইতে হইবে। প্রটোকল সংশোধন অথবা পরিবর্তন করিতে হইলে ঔষধ প্রশাসন অধিদপ্তর/লাইসেন্সিং কর্তৃপক্ষকে লিখিতভাবে জানাইতে হইবে এবং অনুমোদন গ্রহণ করিতে হইবে;

(৩) রিসার্চ সেন্টার অথবা গবেষণা অথবা স্পন্সর অথবা সি.আর.ও. অথবা ক্লিনিক্যাল ট্রায়াল কার্যক্রমের সহিত সম্পৃক্ত সকল পর্যায়ের জনবলের Good Clinical Practice (GCP) গাইডলাইনের উপর প্রশিক্ষণ গ্রহণ করিতে হইবে;

(৪) ইনভেস্টিগেশনাল মেডিক্যাল প্রডাক্ট অবশ্যই বিশ্ব স্বাস্থ্য সংস্থার সি.জি.এম.পি. (CGMP-Current Good Manufacturing Practice) গাইডলাইন অনুসরণপূর্বক উৎপাদন করিতে হইবে। Investigational Product (IP) অথবা Investigational New Drug (IND) অথবা New Chemical Entity (NCE)-এর কোন নমুনা ধ্বংস করিবার ক্ষেত্রে লাইসেন্সিং অথরিটির অনুমোদন গ্রহণ করিতে হইবে;

(৫) ক্লিনিক্যাল ট্রায়াল চলাকালীন অংশগ্রহণকারীদের কোন ঝুঁকি শনাক্ত হইলে ঔষধ প্রশাসন অধিদপ্তর/লাইসেন্সিং কর্তৃপক্ষ উক্ত ক্লিনিক্যাল ট্রায়ালের কার্যক্রম সাময়িকভাবে অথবা স্থায়ীভাবে বন্ধ করিতে পারিবে;

(৬) ক্লিনিক্যাল ট্রায়ালে অংশগ্রহণকারীদের (Participants) অধিকার অথবা নিরাপত্তা অথবা স্বাস্থ্য সুরক্ষার জন্য ক্লিনিক্যাল ট্রায়াল পরিচালনা প্রতিষ্ঠান কর্তৃক Institutional Review Board (IRB) অথবা Institutional Ethics Committee (IEC) গঠন করিতে হইবে। উক্ত Institutional Review Board (IRB) অথবা Institutional Ethics Committee (IEC) ঔষধ প্রশাসন অধিদপ্তর কর্তৃক অনুমোদিত হইতে হইবে;

(৭) ইনভেস্টিগেশনাল মেডিক্যাল প্রডাক্ট আমদানির জন্য ঔষধ প্রশাসন অধিদপ্তরের অনুমোদন গ্রহণ করিতে হইবে। ট্রায়ালে অংশগ্রহণকারীদের নিকট হইতে সংগৃহীত কোন নমুনা পরীক্ষা ও বিশ্লেষণের জন্য বিদেশে প্রেরণের ক্ষেত্রে ঔষধ প্রশাসন অধিদপ্তরের অনুমোদন গ্রহণ করিতে হইবে;

(৮) ক্লিনিক্যাল ট্রায়ালের সময় Adverse Drug Reaction (ADR) অথবা পার্শ্ব-প্রতিক্রিয়া পরিলক্ষিত হইলে স্পন্সর অথবা প্রিন্সিপাল ইনভেস্টিগেটর অবিলম্বে ঔষধ প্রশাসন অধিদপ্তরকে অবহিত করিবে এবং স্পন্সর অথবা প্রিন্সিপাল ইনভেস্টিগেটর ক্লিনিক্যাল ট্রায়ালের পর্যবেক্ষণ ও নিরাপত্তা বিষয়ক প্রতিবেদন নিয়মিত ঔষধ প্রশাসন অধিদপ্তর এর নিকট পেশ করিবে;

(৯) বিদেশি ঔষধ নিয়ন্ত্রণকারী কর্তৃপক্ষ হইতে প্রাপ্ত ক্লিনিক্যাল ট্রায়াল সংক্রান্ত তথ্য অথবা অনুমোদিত ডেটা (data) ঔষধ প্রশাসন অধিদপ্তর গ্রহণ/স্বীকৃতি প্রদান করিতে পারিবে;

তবে শর্ত থাকে যে, প্রয়োজনীয় ক্ষেত্রে ব্রিজিং স্টাডি পরিচালনা করিয়া বিদেশ হইতে ক্লিনিক্যাল ট্রায়ালের প্রাপ্ত ডেটা (data) ভেলিডেট করিবার জন্য লাইসেন্সিং অথরিটি আবেদনকারীকে নির্দেশনা প্রদান করিতে পারিবে।

(১০) ঔষধ প্রশাসন অধিদপ্তর জরুরি স্বাস্থ্যসেবা অথবা মহামারি রোগের নূতন ঔষধের ক্ষেত্রে ফাস্ট-ট্রাক ক্লিনিক্যাল ট্রায়াল (Fast Track Clinical Trial) অনুমোদন করিতে পারিবে; এবং

(১১) স্পন্সর অথবা প্রিন্সিপাল ইনভেস্টিগেটরকে ট্রায়াল সংক্রান্ত প্রয়োজনীয় বাজেট অথবা ফান্ড সম্পর্কিত বিস্তারিত তথ্য ঔষধ প্রশাসন অধিদপ্তর এর নিকট পেশ করিতে হইবে।

(C) ভ্যাকসিনের লট বিমুক্তকরণ (Lot Release of Vaccine):

(ক) দেশে উৎপাদিত ও আমদানিকৃত সকল হিউম্যান ভ্যাকসিন (Human Vaccine)-এর লট বিমুক্তকরণ সনদ (Lot Release Certificate) লাইসেন্সিং কর্তৃপক্ষের নিকট হইতে গ্রহণ করিতে হইবে:

তবে শর্ত থাকে—

(১) বিশ্ব স্বাস্থ্য সংস্থা কর্তৃক প্রি-কোয়ালিফাইড এবং জাতিসংঘের সংস্থার মাধ্যমে সরবরাহকৃত ভ্যাকসিনের উৎপাদনকারী দেশের (Country of Origin) লট বিমুক্তকরণ সনদের ভিত্তিতে লট রিলিজ করা যাইবে;

(২) জনস্বাস্থ্যের জরুরি প্রয়োজনে অথবা দুর্যোগ অথবা আকস্মিক বিপর্যয়কালীন ত্বরান্বিত পদ্ধতিতে কোন নির্দিষ্ট ভ্যাকসিনের লট রিলিজ সনদ প্রদান করা যাইবে;

(৩) পরিস্থিতির গুরুত্ব, সময়ের স্বল্পতা এবং ব্যবহারের জরুরি আবশ্যকতা বিবেচনা করিয়া লাইসেন্সিং কর্তৃপক্ষের পূর্বানুমোদন সাপেক্ষে লট রিলিজ ব্যতিরেকে কোন নির্দিষ্ট ভ্যাকসিন বাজারজাত/সরবরাহ করা যাইবে; তবে পরবর্তীতে লট রিলিজ সনদ গ্রহণ করিতে হইবে; এবং

(খ) দেশে উৎপাদিত অথবা আমদানিকৃত ভ্যাকসিনের লট বিমুক্তকরণের লক্ষ্যে বিশ্বস্বাস্থ্য সংস্থা কর্তৃক প্রি-কোয়ালিফাইড কোন ল্যাবরেটরির পরীক্ষা ও বিশ্লেষণ সনদ গ্রহণ করা যাইবে।

(গ) Research অথবা ব্যক্তিগত ব্যবহারের জন্য সীমিত পরিমান ভ্যাকসিন আমদানির ক্ষেত্রে লট বিমুক্তকরণ সনদের প্রয়োজন হইবে না। তবে সেইক্ষেত্রে আমদানির পূর্বে লাইসেন্সিং কর্তৃপক্ষের নিকট হইতে অনাপত্তি সনদ (NOC) গ্রহণ করিতে হইবে।

০২। যথাযথ কর্তৃপক্ষের অনুমোদনক্রমে জারীকৃত এ পরিপত্র অবিলম্বে কার্যকর হবে।

মোঃ এনামুল হক
অতিরিক্ত সচিব (ঔষধ প্রশাসন)।

মোহাম্মদ ইসমাইল হোসেন, উপপরিচালক (উপসচিব), বাংলাদেশ সরকারী মুদ্রণালয়, তেজগাঁও, ঢাকা কর্তৃক মুদ্রিত।
মাকসুদা বেগম সিদ্দীকা, উপপরিচালক (উপসচিব), বাংলাদেশ ফরম ও প্রকাশনা অফিস, তেজগাঁও, ঢাকা কর্তৃক প্রকাশিত। website: www.bgpress.gov.bd.

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To perform the activities of Pharmacovigilance (PV), Clinical Trial (CT) and Lot Release (LR) more efficiently as per WHA (World Health Assembly) Resolution A67/32, following directives have been made:

(c) Lot Release of Vaccine:

1. Lot Release Certificates of all human vaccines, locally produced and imported, should be taken from the Licensing Authority, provided that,

    a. Lot Release Certificate from the Country of Origin will be acceptable for Lot Release of vaccine(s), if the vaccine is WHO prequalified and procured through UN Organizations;
    b. Fast-track Lot Release Certificate shall be issued in case of Public Health Emergency, Epidemic or sudden disaster;
    c. Upon getting the prior approval from the Licensing Authority, marketing/supply of vaccines will be allowed without Lot Release Certificate considering the urgency of situation, time constraint and necessity of emergency use with; however, Lot Release Certificate of such vaccines shall be obtained afterwards; and

2. Test and Analysis result from any WHO Prequalified Laboratory shall be acceptable for Lot Release of locally produced or imported vaccines.
3. Lot Release Certificates shall not be required for importing limited number of vaccines for research or personal use. But 'No Objection Certificate (NOC)' shall be taken from the Licensing Authority before import.

This Circular will be effective immediately.

Md Enamul Haque
Additional Secretary (Drug Administration)

Note: Translated only (c) Lot Release of Vaccine

13. Reference Documents

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13.13 Health Product Policy and Standards (HPS). (2003, June 1). *TRS 908 - 37th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Accessed on August 2024. Available at: https://www.who.int/publications/i/item/WHO_TRS_908

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End of the Document

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