Q U A L I T Y M A N U A L

National Control Laboratory

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1. INTRODUCTION

In 2003, Ministry of Health and Family Welfare (MOHFW) declared Drug Testing Laboratory (DTL), Dhaka as National Control Laboratory (NCL) and Directorate General of Drug Administration(DGDA) as National Regulatory Authority (NRA) for vaccines and biological products. At present the activities is performed by newly established NCL. The National Control Laboratory has taken it as a primary duty as per article 18 of the National Constitution, to ensure the potency, safety and efficacy of these types of products to meet the national requirement set by the National Regulatory Authority. Directorate General of Drug Administration is given the responsibility for this purpose.

- The functions of both NRA and NCL required to be backed by appropriate laws
- NCL may be given the authority by law to review available clinical, safety, potency and efficacy data and use other relevant information from the producer in any country.
- Network of NCLs of different countries may be encouraged, that will result in technological maturity of the NCLs of importer country.
- To help the post marketing surveillance, NCL may analysis the complaint sample, and send the report to DGDA & concern authority.
- NCL should develop a written procedure for rapid lot release and efficient recall in case of any mishap after immunization.

Lot release is a process of approval of a particular product to market after a through reviewing the manufacturing process of that product. This process is carried out for vaccines and other biological in most of the countries. The production data, in-process quality test results and sometimes verification of QC test results is considered by the NCL as a requirement for issuance of lot release certificate. As vaccines are complex biological

molecules having inherent variability of systems, each production run of such product are considered unique. Therefore these vaccines are subject to scrutiny by NCL on a lot-by-lot basis.

The independent control of vaccine lots is important as vaccines are given to a large number healthy infants and children and therefore must be safe and effective.

National Control Laboratory will perform the Lot Release of Vaccines and biological Products within the framework of Drug Act of Bangladesh. US and EU guidelines may be followed in applicable cases. Indicators of lot release as suggested by WHO for the regulatory functions of NCL are as follows:

Lot release be based on

- A protocol review as a part of specification for procurement and lot release certificate from NRA or NCL of the country of origin,
- Written procedure and criteria for lot release process (checklist, sampling guidelines)
- Access to product files, NCL report and inspection reports and complaints in case of problems.
- Records kept of lot release data for analysis of consistency of quality and continual review and scientific dialogue with manufacturers on issues of quality test results
- Written criteria for exemption from lot release if any.

2 PURPOSE

The main aim of the National Control Laboratory is to have safe, potent and efficacious Vaccine & biological in the country. To achieve this goal, NCL performs tests & assays to ensure that a particular product complies with the requirements and specifications

established and approved by National Control Authority during registration and licensing process. It is most important to have reliable, reproducible results and all the agencies should have confidence in the laboratory results of NCL. For this, accreditation of the Laboratory at each step of its performance is warranted and Laboratory Quality Manual is important component of this process. The Quality Manual describes the quality assurance program used in National Control Laboratory and sets out the established requirements to competently and effectively achieve the program objectives of the National Control Laboratory. The main objectives of the laboratory which are achieved with the help of Quality Manual are out lined below:

- To have quality vaccines.
- To detect deviations.
- To correct errors.
- To improve efficiency.
- To reduce costs.

For this, accreditation of the Laboratory at each step of its performance is warranted and Laboratory Quality Manual is important component of this process.

3. Scope & Objective

The quality manual defines the the assessment of quality, efficacy, potency, toxicity or contraindication of any vaccines, biological and biotechnological products produced in the country or imported from any producer country with a view to ensure a safe and effective use by the consumer.

4. Terms and Definitions

Accreditation- a formal recognition that a laboratory is competent to carry out specific tests or types of tests or calibrations.

Calibration **-** a set of operations which establish, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, or values represented by material measure, and the corresponding known values of a measured. Also: comparison of a measurement standard or instrument with another standard or instrument to detect, correlate, report, or eliminate by adjustment any inaccuracy of the compared.

Corrective Action **-** an action taken to eliminate the causes of an existing deficiency or other undesirable situation in order to prevent recurrence.

Deficiency **-** the non fulfillment of WHO conditions and/or criteria for accreditation.

External Audit **-** Appraisal of a testing laboratory by an outside body, using specified criteria and checklists to evaluate compliance for accreditation.

Good Laboratory Practices (GLP) **-** an acceptable way to perform some basic operation or activity in a laboratory that is known or believed to influence the quality of its outputs. GLPs ordinarily are essentially independent of the measurement techniques used.

Internal Audit **-** the process of self appraisal of a testing laboratory using specified criteria and checklists to evaluate compliance for accreditation; may be used as a quality management review as well.

Interlaboratory Comparisons **-** Organization, performance, and evaluation or tests on the same or similar items or materials by two or more laboratories in accordance with predetermined conditions.

On-Site Assessment **-** a formal examination or official inspection of a calibration or testing laboratory to evaluate its compliance with specific laboratory accreditation criteria.

Proficiency Testing **-** the determination of laboratory performance by means of comparing and evaluating tests on the same or similar items or materials by two or more laboratories in accordance with predetermined conditions.

Standard, Reference **-** A standard, generally of the highest quality available at a given location, from which estimations made at that location are derived.

Standard, Secondary **-** a standard whose value is assigned by comparison with a primary standard of the same quantity.

Standard, Working **-** a standard, usually calibrated against a reference standard, which is used routinely to calibrate or check material measures or measuring instruments.

Standard Operating Procedure (SOP) **-** a procedure adopted for repetitive use when performing a specific measurement or sampling operation. It may be a standard method or one developed by the user.

Internal Quality Assessment (IQA)- Internal QC is the set of procedures undertaken by the competent personnel of a laboratory for continuously and concurrently assessing laboratory works and the emergent results to decide whether they are reliable enough to be released. It is a part of in-house quality assessment. Samples are prepared, distributed, evaluated and results are assessed internally.

External Quality Assessment (EQA): External quality assessment is a system of assessing the laboratory performance with a defined objective by an outside agency. Both internal and external quality assessment are complementary in ensuring the reliability of procedures, their results and finally the quality of the product.

5. Status of the Laboratory

5.1 Legal status:

Drugs Testing Laboratory acts as National Control Laboratory for vaccine & biological in Bangladesh declared in 2003. This laboratory is established under the Drugs Act, 1940 and Rules there under. At present NCL is functioning independently under the supervision of DGDA since 07.06.2010. Its activities for testing and issued pre-release certificate of all vaccine & biological which are marketed in Bangladesh (produced & procured). It also provides support to National Regulatory Authority during registration and licensing process as its technical body.

5.2 Testing is of International Competence:

The laboratory is committed to ensure the release of only safe and efficacious Vaccine & biological meant for human use. The laboratory carries out the testing of Vaccine & biological as per the International /National and WHO guidelines, so as to meet and satisfy the needs of the ultimate customers/consumers i.e. the user population. The laboratory has the testing standards of international level, which are evidenced by WHO's regular audit assessments.

5.3 Location of the Laboratory and its testing facilities:

The National Control laboratory is located the campus of Institute of Public Health and works independently under the supervision of DGDA.

Very recently as per WHO recommendation, MOH&FW placed Drug Testing Laboratory under Directorate General of Drug Administration (DGDA) as per orders No. 45.160.116.00.00.003.2010-166 dated 07.06.2010 which previously was under the administrative control of Directorate General of Health Service (DGHS). Though the department is currently working under DGDA, the all staff of DTL & NCL are getting salary and logistic support from the existing budget of IPH.

5.4 Independent Judgment on quality of Vaccine & biological:

The laboratory is a Third party testing laboratory and has independent opinion on the quality of the vaccine & biological, according to Drug act, 1940 and Bengal Drugs Rules 1946.

The laboratory has complete independence of judgment because of its legal status.

5.5 Minimization of Departures from the laboratory and management System:

The laboratory has the trained human resource, working in the laboratory for a reasonable period of time. This is evident from the list of the trained staff and their service with the laboratory**.** The status of the laboratory and its responsibility for the society, imparts job satisfaction, which helps in minimization of departure from their laboratory. The personnel working in the laboratory are free from any internal or external pressures and are committed for work of high quality.

5.6 Confidentiality of information:

The laboratory maintains the confidentiality and proprietary rights of all information including type of work performed and results of tests to the extent allowable by law. It functions under the Drugs Act, 1940 and Bengal Drugs Rules, 1946.T he laboratory ensures confidentiality of the testing and its subsequent results to the other customers. All officials working in NCL are governed by **Bangladesh Services Rules (BSR)**. All officials are bound by the oath they take at the time of induction into service.

5.7 No person in the laboratory can advice /act as consultant to any manufacturer. The decision of Govt. Analyst / Deputy Chief will be final on the quality of the product under consideration.

5.8 The laboratory is located in the campus of Institute of Public Health and works independently. The finances of the Laboratory are supported by Ministry of Health and family Welfare, Bangladesh under the supervision of DGDA of the vide its orders No. 45.160.116.00.00.003.2010-166 dated 07.06.2010.

5.9 The Govt. Analyst and DC are responsible for ensuring that testing is carried out by only the competent and trained personnel. Every test method is authenticated by the Govt. Analyst/ and DC, Drug Testing Laboratory (NCL). They are also responsible for ensuring that the resources are made available for high quality of laboratory operations.

5.10 Organization structure

Organogram on page 59

6. Responsibility

6.1 Deputy Chief

- The Deputy Chief is responsible for the overall compliance of the laboratory to this Quality Manual.
- implements and enforces the applicable good laboratory practices describe in reference documents;
- provides resources, adjusts workloads, and provides training opportunities for laboratory staff to facilitate completion of assigned tasks in a safe work environment consistent with test requirements and personnel capabilities; and
- assigns deputies for both the technical and quality managers in the case of an absence.

6.2 Assistant Chief/Assistant Director

- is responsible for the overall administrative and technical operations of the laboratory;
- specifies and/or approves all methodologies used;
- also acts as Quality Control Manager

- implements good laboratory procedures by providing instruction and training as needed, develops work plans and procedures, and requires that these be followed in all day-to-day operations;
- assigns only competent personnel to complete tests;
- attests, by signature, to the validity of all laboratory tests and reports
- ensures continued accreditation of the laboratory.
- maintains, analyzes, and updates statistical data and/or control charts;
- participates in available and relevant proficiency tests, round-robins, and/or inter laboratory collaborative studies;
- Where necessary, identifies, develops, and implements improvement of the laboratory procedures, department programs;
- maintains the quality manual;
- has direct access to Deputy Chief.

6.3 Deputy Chief for the key managerial functions:

Deputy Chief is designated as the Deputy Quality Control Manager. He is responsible for assisting the QC. Manager in his routine activities and looks after the duties of the Quality Control Manager in his absence. Similarly for every technical; operation deputies are appointed.

6.4 All the personnel in the laboratory are made well aware of their duties, its importance and their contribution for continual improvement of the laboratories performance at the time of induction into the laboratory. Every person in the laboratory is free to approach to the Deputy Chief for any kind of suggestion / grievance. The management is committed for satisfactory resolution of the situation.

6.5 Government Analyst

DUTIES OF GOVT. ANALYSTS (RULE-45)

(1)The Govt. Analyst shall cause to be analyzed or tested such sample of drugs and vaccines as may be sent to him by Inspectors or other persons under the provisions of Drugs Act, 1940 and Bengal Drugs Rules, 1946.

(2) A Govt. Analyst shall from time to time forward to the Government reports giving the result of analytical work and research with a view to their publication at the discretion of Government.

(3) PROCEDURE ON RECEIPT OF SAMPLE (RULE-46)

On receipt of a package from DGDA/ an Inspector /AFFDL/ Police/RAB/IPH/CMSD/Veterinary dept./containing a sample for test or analysis, the Govt. Analyst shall compare the seals on the packet or on portion of sample or container with the specimen impression received separately and shall note the condition of the seals on the packet or on portion of sample or container. After the test or analysis has been completed, he shall forthwith supply to the Inspector a report in triplicate in Form 13 of the result of he test or analysis, together with full protocols of the tests or analysis applied.

(4) PROTOCOLS OF THE TESTS OR ANALYSIS APPLIED

1) For pharmacopoeial drug, where the tests or methods of analysis prescribed in the official pharmacopoeia are followed, references to the specific tests or analysis in the pharmacopoeias are given in the report; For patent or proprietary medicines for which the tests and methods prescribed in any of the official pharmacopoeias are applicable and are followed, references to the specific tests or analysis in the pharmacopoeias are given in the report;

(1) For patent or proprietary medicines containing pharmacopoeial drugs for which the official tests or analysis or methods of assays are modified and applied, a description of the actual tests or, as the case may be, analysis or methods of assays so applied is given in the report; For patent or proprietary medicines for which no pharmacopoeial tests or method of analysis are available but given in standard books or journals, reference to the same from which the tests or methods of analysis have been adopted, should be given in the report;

(2) For those drugs for which methods of test are not available and have been evolved by the Government Analyst, a description of tests applied is given in the report.

(5) FURNISHING "PROTOCOLS OF TEST APPLIED"MANDATORY

In view of the provisions of Rule 46 which are mandatory, the Government Analyst is bound to furnish to the Inspector the full protocols of the tests applied.

(6) REPORTS OF GOVT. ANALYST

(1)The Government Analyst to whom a sample of Any drug, vaccine and biologicals has been submitted for test or analysis under part –V, Section 47, shall deliver to the Inspector a signed report in triplicate in the prescribed form 13 as per Drug Acts 1940.

(2)The report signed by a Govt. Analyst under this Chapter shall be conclusive unless the person from whom the Sample was taken, has within twenty-eight days of the receipt of the report, notified in writing the Inspector or the Court before which any proceedings in respect of the sample are pending that he intends to adduce evidence in controversion of the report.

6.6 Analyst

- To act as Unit-in-charge and report to Officer-in-charge / QC. Manager.
- To supervise the activities of microbiology section, Pharmacological section, chemical analysis
- To Maintain & ensure clean room activities
- Training for manpower development
- To supervise animal house & Lab animal
- Method development & validation
- Documentation of Chemical analysis

6.7 Assistant Analyst

- To co-ordinate activities related to testing and assigning of duties to the staff (e.g. Samples distribution, testing & documentation) & documentation of a particular unit.
- To check product summary files / product dossiers, summary protocol, review check lists.
- To test vaccine samples.
- Correspondence matters and writing the document for quality system (e.g. Sops, Check lists, Study plans)
- Observation of tests under progress and final test results.
- Responsible for the maintenance of the laboratories equipments and testing & animal facility of a particular unit.
- To perform internal audits and conduct departmental meetings.
- To coordinate the research projects, related to the products of concerned units.

- Responsible for maintenance & archiving of all records related to the products & sample storage.

6.8 Medical Technologist/ Senior Technical Assistant

- Reporting to the unit-in-charge regarding analysis and other laboratory issues.
- Testing of samples as asked by unit- in-charge to do so.
- Preparation of draft documents and letters.
- To assisting unit-in-charge for conducting product specific meeting.
- To assist in the activities of analysis record preparation & maintenance.
- To assist in the activity related to sample distribution and storage date analysis and:
- Maintenance of temperature records of equipments.

7. Management system

7.1 Quality policy

-The laboratory will carry out the testing of Vaccine & biological at par with the International standards.

- The testing will be done as per International, National and WHO guidelines.
- To meet and satisfy the needs of the ultimate customers/consumers i.e. the user population of vaccines and antisera; is our aim.

-The laboratory will conduct all assays under ideal conditions and by using techniques that are conducive to a high degree of reliability and follows generally recognized good laboratory procedures.

- It is our policy to provide the highest quality services attainable, to manufacturers, port health authorities, drugs control authorities of state and centre, through

continual improvement of the quality system.

- High Quality in services will always be a constant effort and focus.

The quality policy is Authorized by the Deputy Chief of National Control Laboratory (NCL) and approved by the Quality Control Manager.

7.2 Tests

The laboratory conducts tests for the parameters in accordance with the procedures, practices, and conditions required, recommended, and/or approved as per pharmacopeias and WHO technical report series and/or its affiliated documents. The techniques utilized for specific tests ensure the accuracy, tolerance, precision, traceability and are within the applicable guidelines. All tests are conducted as per study plans**.**

Lot Release of Vaccines is done as per World Health Organization Criteria of National Regulatory Authority function of **Lot release** and testing is done as per criteria of **Laboratory Access.**

7.3 The guidelines for the accurate performance of the tests are available in the form of controlled copies of the Sops. These are available with the concerned Unit-in-Charge and QC.Mangaer. The Govt. Analyst and DC are responsible for ensuring that testing is carried out by only the competent and trained personnel. Every test method is authenticated by the Govt. Analyst and DC of National Control Laboratory (NCL). They are also responsible for ensuring that the resources are made available for high quality of laboratory operations.

7.4 This quality manual (along with appendices and references) is available to all laboratory staff and all staff familiarizes themselves and complies with the policies and procedures established in the manual and associated documents.

7.5 Independence

It is ensured that the laboratory is independent from any commercial, financial, or other pressures which might adversely affect the quality of tests and resulting reports. Policy provides guidelines to ensure laboratory independence. The laboratory is established under the provisions of Drugs Act 1940 and rules there under.

7.6 Accreditation

Accreditation of a Laboratory by the Accreditation Committee is essential and mandatory. Accreditation is an approved procedure by the Accreditation Committee, which is competent enough to function as a regulatory authority to accord formal recognition to a laboratory to undertake specific task, provided that the laboratory meets predefined standards. ISO 17025 defines the standards of accreditation of a laboratory. It is a process of inspection of laboratories and their licensing. National Control Laboratory has to ensure conformity to predefined criteria pertaining to various aspects of infrastructure and functioning. After accreditation the National Control Laboratory, will take part in inspection of a laboratory with NRA.

7.7 Confidentiality and proprietary rights

The laboratory maintains the confidentiality and proprietary rights of all information including type of work performed and results of tests to the extent allowable by law. It functions under the Drugs Act, 1940 and the Bengal Drugs Rules, 1946. All laboratory personnel and staff are informed of this policy. All officials working in NCL are governed by **Bangladesh Services Rules (BSR)**. All officials take oath at the time of induction into service.

7.8 Delegation of authority

At times that DC, Officer-in-Charge or Quality Control manager is not available; a temporary arrangement has to be made immediately.

7.9 Conflict of interest

Staff working in NCL will not have any financial interest which might compromise the integrity and credibility of NCL. All the staff working in NCL will disclose any private financial interests that are related to National Control Laboratory activities. All staff are governed by **Bangladesh Services Rules (BSR).**

7.10 Operation control

Deputy Chief of the Laboratory keeps track of all the activities going on in the various sections including safety, security, training, testing, interpretation and assessment of test results.

7.11 Deviations

From time to time it may be necessary to authorize deviations from the requirements stated in this manual. Such deviations must be authorized by QC Manager and DC of the vaccine Department of NCL.

8. Document & records Processing

Processing records of biological production must include the manufacturing history of each lot of a product showing that it has manufactured, tested, dispensed into containers and

distributed according to a licensed procedure. This processing record contains the following information:

- The name and dosage of the product;
- The lot identification number and the date of manufacture
- The complete formulation of the lot, including identification of seed and starting mater.
- The batch number of each components used in the formulation
- The yield obtained at different stages of manufacture of the lot
- A duly signed record of each step followed, precautions taken and special observation
- A record of all in process control tests and results
- Identification of packaging materials, containers and a specimen of label
- A dated signature of the expert responsible for approval
- A compliance report registered with NCL should be dated and signed by expert
- A record of decision given by the NCL if needed.

Authority

The Quality Control manager has the designated authority to modify or update the Quality Manual. The quality manual is annually reviewed and updated after 2 (two) yrs. The Deputy Chief of the laboratory is responsible for final approval of all changes made to the quality manual and the revised document takes effect when signed by Deputy Chief of the Laboratory.

This quality manual is made available to all laboratory staff and all staff familiarizes themselves and complies with the policies and procedures established in the manual and associated documents.

Controlled Copies

Controlled copies of this quality manual, all SOPs, study plans, checklists are made available to all ATOS and Technical Supervisors. All controlled copies are numbered and updated by the Quality Control Manager whenever changes are made. Recipients of controlled copies are issued the revised quality manual with a cover sheet identifying updates made to the manual. It is the responsibility of the quality manager to ensure that the most current quality manual is issued and followed by all laboratory and administrative staff. A list of the names, control numbers, and locations of all controlled copies is maintained in the laboratory files.

Document Changes:

- The documents will be reviewed at least once a year. The reason for altering any document will be recorded in the History sheet available with every document.
- The altered or the new document will be given a new version number.
- Corrections are made to data by drawing a single line through the entry and initialing the change, with a note as to why the change was made. The change is made in all the controlled copies also. With the annual revision of the document, a new version number will be given to the whole document in which correction has been made.

9. Review of requests tenders and contracts:

Any work pertaining to the testing of samples is carried out according to Drugs Act 1940, WHO and Standard Pharmacopoeial Guidelines.

The laboratory has the capability and resources to meet the client's requirements.

The laboratory has a system to review the request of clients.

Records of reviews, including any significant changes, are maintained. Records of any discussions or meeting with the customers are also maintained.

The requirements, including the methods to be used, are adequately defined and documented.

10. **Control of nonconforming testing and / or calibration work**

10.1 If a result of test or testing procedure does not conform to its own procedures or in-house specifications of the manufacturer or pharmacopoeial specifications, Deputy Chief of the Department is informed and accordingly action is initiated

10.2 Test is repeated as per retest policy of the department.

10.3 Results of all valid assays are taken before taking the decision to declare the results as nonconforming.

11 Improvement:

The laboratory is committed to continually improve the effectiveness of its management system through the use of the quality policy, quality objectives, audit results, analysis of data, corrective and preventive actions and management review.

12. Control of records

12.1 The laboratory ensures the safety and security of records. Records include those with information required by regulation, or associated with original test observations, calculations, and reported results. Test results in the form of raw data are recorded in permanent form, in bound notebooks, or on standard forms on file. Permanent ink is used to record the actual data and no erasures or white-outs are made. Corrections are made to data

by drawing a single line through the entry and initialing the change. Test records contain sufficient detail to, if necessary, permit the repetition of test. Records of original data include the following:

12.2 Standard Operating Procedure (SOP) used;

12.3 Description of, and reason for, any deviation from the SOP;

12.4 Identity of the personnel performing the test;

12.5 Identity and description of samples under test;

12.6 Identity of equipment or apparatus used;

12.7 Identity of standards used and reference to traceability;

12.8 Date of test;

12.9 State test number;

12.10 Environmental data during test, when applicable ("Accommodation and Environmental conditions");

12.11 Records, including those in computer files, are accessible to authorized personnel only. Computer files are backed-up for protection against loss.

12.12 Records maintained by the laboratory are in three categories: administrative, test-related, and process measurement assurance. The laboratory maintains and retains the records in the locations stated for the specified amount of time. All records are maintained as per drugs rules.

12.13 All records are retained **for at least one year after the expiry of the finished product** as per GMP WHO guideline.

12.14 Reference samples are retained **for a period of three months after the date of expiry** as per GMP WHO guideline.

13. Audit

13.1 Internal Audit

Internal audits (self-assessments) are conducted at least once a year to verify that operations continue to comply with the quality system. Auditors are trained in auditing techniques, have technical insight concerning the laboratory's functions, and are (wherever possible) independent of the activity to be audited. When audit findings cast doubt on the correctness or validity of the laboratory's test results or some observations are made, the Officer-in-Charge investigates further and, if warranted, directs immediate remedial measures. A compliance report is given to the auditor and the Quality Control Manager.

13.2 The laboratory has established and maintains a quality system supporting the tests conducted by the laboratory. The quality system is described in these quality manual, appendices, and applicable sections of the references named therein. These documents are readily available to all laboratory staff and serve as the basis for evaluating the tests and associated reports. The laboratory conducts internal audits or periodic checks carried out by or on behalf of management to ensure that the laboratory's policies and procedures as set out in the quality manual are being followed.

13.3 Quality System

- The basic elements of the quality system include the use of
- Qualified personnel for each test or assay
- Supervision and review by senior personnel
- Approved methodology including standard operating procedures, and assay validation

- Appropriately maintained and calibrated standards, equipment, and associated apparatus.
- Environmentally controlled facilities and/or proper accounting of relevant environmental factors.

13.3.1 Quality Control

- Quality Control of Vaccine & biologicals (Vaccines and Sera) imported, indigenously produced or to be exported.
- Advice to NCL on technical matters and interaction with manufacturers for improvement in the quality of Vaccine & biological.
- Scrutiny of manufacturer's protocols as per the checklists prepared.
- Preparation of IP Monographs, quality Control Protocols and Manuals.
- Evaluation of dossiers of manufacturing and quality control of Vaccine & biological.
- Pre-licensing control testing for assuring consistency of production.
- Development, evaluation, establishment and implementation of testing procedures.
- Review of reports on quality defects and provision of advice on withdrawals.
- Participation in licensing process.
- Research and development in the field of quality control of Vaccine & biological.

13.3.2 Preparation of Reference Standards

National Reference Standards will be prepared and calibrated against International Reference Standards and supplied to various manufacturing and testing Laboratories/ Institutions in the country for maintaining uniformity in the production and testing of Vaccine & biological**.**

13.3.3 Collaborations

Co-ordination and collaboration with International agencies like WHO, UNICEF, PAHO and National Control Laboratories of various countries.

13.3.4 Training Courses

Conduct courses on quality control of Vaccine & biologicals for National and International participants. Global Training Network Centre for Lot Release.

13.4 Quality Audits and Review

The basic elements of the quality audit and review program include:

- Identification of problems which arise as a result of any client-discovered errors and/or, discrepant results from the analysis of the laboratory test data
- Evidence from internal audits and trend analysis. Control charts or trend analysis are done on regular basis and conclusions drawn for any remedial action and
- Evidence from external audits, participation in proficiency tests, inter laboratory collaborative experiments.

13.5 Review of Accreditation Material

The laboratory is visited regularly by WHO experts for discussions. Accreditation or review is dependent upon two NRA functions.

13.6 External Audits

External audits (on-site assessments) are performed by WHO / NRA to verify that the laboratory's operations, facilities, equipment, standards, and staff continue to comply with the guidelines and this Quality Manual. All external and internal audit and accreditation review findings, and any corrective actions that arise from them, are promptly settled within the agreed time, documented by the quality manager, and maintained in the laboratory files. Compliance report is sent to the concerned authority.

14. **Management reviews:**

14.1 Management shall periodically conduct a review of laboratory's management system and testing and / or calibration activities to ensure that the system is in place and to introduce necessary changes or improvements. The review shall look into:

14.1.1 Policies and procedures.

14.1.2 Review of Reports of technical and scientific staff.

14.1.3 Outcome of recent internal and external audits.

14.1.4 Complaints.

14.1.5 The results of inter-laboratory comparisons or proficiency tests.

14.1.6 Customers feed back.

14.1.7 Changes in the quantum and type of work.

14.1.8 Corrective and preventive action.

14.1.9 Recommendations for improvement.

14.2 The decisions taken in the management review meeting are implemented in the pre determined/targeted time schedule for effective working of the laboratory.

15. Technical Requirements

15.1 General

15.1.1 Many factors contribute to the accuracy and reliability of the tests and / or calibration performed by a laboratory. Following factors may be contributed to the outcome of results:

- Infrastructure.
- Human factors (Personnel).
- Accommodation and environmental conditions.
- Test and calibration methods and method validation.
- Equipment
- Measurement traceability
- Sampling.
- Handling of test and calibration items.

15.1.2 Personnel

15.1.2.1 Laboratory staff is selected for employment based on professional qualifications, including education and relevant experience. All scientists are recruited directly through Public Service Commission on the basis of framed recruitment rules. Technical staff is recruited through DGDA on the basis of written examination and interview following an initial screening process.

QUALIFICATION OF GOVT. ANALYST

As per Part-V, Section 44, Sub-section (a,b,c),Drugs Act 1940, a person appointed as a Govt. Analyst under the Act shall be a person who :

a) i) MBBS ii) B.Pharm iii) Degree in Pharm. Chemistry

And

Not less than 3 years' post graduate experience in the testing of Drugs in a laboratory under the control of:

i) A Govt. Analyst appointed under the Act or

ii) The Deputy Chief of an Institution or Testing Laboratory approved for the purpose by the appointing authority or

iii) Has completed not less than three years' testing of drugs, vaccine and biologicals in NCL.

iv) Who can produced evidence of satisfactory training in Physiology, Bacteriology, serology and Pathology.

b)

i) Possess a post-graduate degree in medicine or science or pharmacy or pharmaceutical chemistry or Associate ship Diploma of the Institution of Chemists (AIC) obtained by passing the said examination with 'Analysis of Drugs and Pharmaceuticals' as one of the subject.

And

For testing of Antisera, Toxoid, Vaccines and Diagnostic Antigen for veterinary use i) B.V.Sc

ii) B.Sc

iii) B. Pharm

vi) MBBS

And

Not less than 5 years' experience is required for graduate degree holder and not less than 3 years experience is required for post-graduate degree holder in the standardization of Biological Drugs.

Staffing is just sufficient to maintain the timely processing of workload, laboratory internal monitoring, quality control, and traceability activities required for accreditation.

15.1.2.2 Adequately trained staff is a key factor in performing the tests. Laboratory personnel have the necessary background in the life sciences to ensure comprehension of the laboratory tests and operations. There is a provision for external training through WHO and on-the-job training for the scientific and technical staff.

The Deputy Chief and Officer-in-Charge, utilizing staff resources to meet policy goals:

- Implement and apply the procedures contained in the referenced documents as per list**;**
- Provides ongoing training to ensure proficiency in testing;
- Develops work plan schedules and requires that the staff follow the procedures in day-to-day operations; and
- Assign tasks based on personnel training and verified competence.

15.3 **Training Requirements**

NCL requires and provides training to all staff and personnel from outside. Laboratory staff meets the training requirements of NCL and all training is documented and maintained in the laboratory. Laboratory staff conducting experiments in the specific areas has successfully completed the noted courses and assignments as per the training requirements of the department. All the technical personnel have long years of experience in quality control of Vaccine & biologicals. Training is imparted as per **Training manual.**

15.4 Accommodation and Environmental Condition:

15.4.1 Facilities and Conditions

15.4.1.1 The laboratory facilities are maintained, where applicable, in accordance with Good Laboratory Practices. The design of the laboratory does not adversely affect the assay results and supports good laboratory practices.

15.4.1.2 The laboratory facilities, test areas, energy sources, lighting, heating, and ventilation facilitate proper performance of estimations and tests. The laboratory ensures that dust, electromagnetic interference, humidity, line voltage, temperature, sound and vibration levels or temperature changes that adversely affect the estimations are appropriate for specific results.

15.4.1.3 The environment in the laboratory where testing is performed does not invalidate results nor adversely affect the accuracy or uncertainty of the

measurement. Laboratory staff ensures adequate conditions in the facility by items listed below:

- Verify that lighting and heating are controlled and monitored.
- Maintain good housekeeping practices to promote a clean, uncluttered laboratory according to procedures list**.**
- Have sufficient space to minimize the risk of injury to staff and/or damage to standards or equipment due to activities around test setup.

15.4.2 **Environmental Conditions :**

15.4.2.1 Cell culture Laboratory:

Environmental conditions are monitored on regular intervals by exposing agar plates for colony forming units and by air sampling. Monitoring of temperature and humidity of the laboratory is done on regular basis.

A clean zone is a defined space in which concentration of airborne particles is controlled to specified air borne particulate cleanliness class.

Classification	Total particles > 0.5 m / m^3	Total particles > 0.5 m / m^3	cfus per m^3
A^+	3500	0	< 1
B	3500	0	5
C	350000	2000	100
D	3500000	2000	500

Clean Room Standard According to European Pharmacopoeia

It is necessary to assess the microbial levels in the air and on the surface of the Clean rooms to control the bio-contamination. Microbial levels of process water and gases, raw materials and final products must be monitored in a regular basis as well as monitoring microbial levels of the personnel working in the area. All solutions and media used throughout the production process must be tested for microbial load. This can be done through bio-burden testing and total viable air borne count.

15.4.2.2 Sterility Testing Laboratory:

Environmental conditions such as temperature and humidity are recorded daily. Environmental conditions are monitored on regular intervals by exposing agar plates for colony forming units and by air sampling.

Grade	**Air, cfu per m^3**	**Surfaces, cfu per contact plate USP (55 mm)**	**Settle plates, cfu per 4 hours (90 mm.)**	**Gloves, cfu per contact plate(5 fingers)**	**Masks, Boots & Gowns, cfu per contact plate**
A	< 1	< 1	< 1	< 1	---
B	10	5	5	5	---
C	100	25	50	---	---

A clean room environment is controlled environment to meet a specified cleanliness class in terms of airborne particles and microorganisms.

15.4.3 Test and calibration methods & method validation:

This is done as per SOP No.NCL-GPL-012 which describe Master plan of assay validation and validation of a new test as per SOP No.NCL-GPL-013 respectively**.** There are product specific sop for respective products.

15.4.3.1 The laboratory maintains administrative and test-related procedures in the laboratory files. These procedures are available to the laboratory staff and are followed to ensure the integrity of administrative duties, calibrations, and test results (Procedures List). Equipment manuals, operating instructions, reference data, specifications, and tolerance tables relevant to laboratory tests are maintained in an up-to-date file in the laboratory, and are readily available.

15.4.3.2 Appropriate checks of data, calculations, and test results are made by the laboratory staff to ensure that procedures are followed and to ensure assay reproducibility. Records are maintained regarding feedback and corrective action, whenever testing discrepancies are detected. Procedures for feedback and corrective actions are maintained in the laboratory.

15.4.3.3 Administrative-Related Procedures

Procedures are maintained for the purchase, reception and storage of consumable materials used for the technical operations of the laboratory.

15.4.4 Computer Software Procedures

15.4.4.1 Where computers are involved in data recording, retrieval, processing, calculation, analysis, or reporting, the laboratory ensures that:

- The requirements of this manual are maintained; and
- Computer software has been documented and verified for use.

15.4.4.2 Procedures are established to:

- Protect the integrity of stored data;
- Provide limited access to maintain security of the programs in use;

  Back-up programs and records; and
- Provide information for revising the software if updates occur.

15.4.5 Selection of methods:

15.4.5.1 Laboratory shall use compendial (Standard) methods for the test and analysis.

15.4.5.2 These compendial methods are mentioned in the pharmacopoeia of respective countries in which the product is manufactured.

15.4.5.3 The manufacturer of the product specifies the standards applied.

15.4.5.4 These procedures are also in the form of technical guidelines of World Health Organization or in some cases National guidelines.

15.4.6 Non Standard Methods:

When it is necessary to use methods, not covered by Standard methods, these shall be Validated before use.

15.4.7 Validation of methods:

15.4.7.1 The laboratory shall validate non standard methods, standard methods used outside their intended scope, and amplification and modification of standard methods to confirm that the methods are fit for the intended use.

15.4.7.2 Methods are validated as per **SOP no.----------**

15.4.7.3 The techniques used for the determination of the performance of a method should be one of , or a combination of the following :

- calibration using reference standard or reference material.
- comparison of results achieved with other methods.
- Inter laboratory comparisons.
- WHO collaborating studies and proficiency testing
- Trend analysis with statistical evaluation of results.

15.5 Equipment

List of all equipments and their calibration status is maintained in the laboratory

Requirement for qualification should be applied to equipment used in production as well as in quality control laboratories.

The Design Qualification (DQ) should define the functional and operational specifications of the instrument and should detail the conscious decisions in the selection of the supplier.

Priorto use and to ensure that the equipment is fit for its intended use the different stages of qualification should be performed, e.g. IQ, OQ, and PQ.

In addition, the equipment should be well maintained and routinely calibrated. The supplier or a third party may do certain stages of the equipment qualification. Each major piece of equipment should have a logbook, which should detail at least, the supplier's name, module, model and serial number, date of installation, all qualification performed, maintenance performed and reference to records, and routine use.

15.5.1 Log Books. Each equipment has a log book which contains the following information :

- Equipment no;
- Equipment SOP no;
- Location of Equipment;
- Whether calibration / validation certificate provided by external agency / Or
  by CRI workshop;
- Frequency of calibration;
- Performa no. for daily records;
- Location of records;
- Equipment failure record / incident report;
- Equipment inspected by workshop if any;
- Equipment repair record if any;
- Revalidation / calibration after repair;
- Equipment cleaning / checking calibration / validation record

15.5.2 Operation and Maintenance

15.5.2.1 Equipment and Associated Apparatus

- Laboratory equipment is properly maintained in accordance with procedures for calibration, verification, and maintenance. These procedures are located in the laboratory files.
- Any item of the equipment which has been subjected to mishandling or which gives suspect results or has been shown by verification or otherwise to be defective is taken out of service, clearly identified, and whenever possible stored at a specified place until it has been repaired and shown by calibration, verification, or test to perform satisfactorily. The laboratory examines the possible effect of defected equipment on any previous calibrations.
- Operation manuals and instructions for proper maintenance of equipment are available to the staff and located in the laboratory.
- Newly installed equipment are tested to verify that they perform satisfactorily before they are placed into service. The laboratory maintains procedures for testing newly installed equipment.
- Equipment is used or operated only when in a safe and reliable condition, by personnel who have been trained and are qualified.

15.5.3 Maintenance & Calibration Policy:

15.5.3.1 All the newer equipments purchased are to be subjected to installation qualification (IQ), Operational qualification (OQ) and performance qualification(PQ).

15.5.3.2 Validation/Calibration certificates are to be required for all newer equipments.

15.5.3.3 All the equipments are to be covered under a preventive maintenance (newer & existing) program (PMR) to be executed every six months.

15.5.3.4 Regular checkup & calibration is to be ensured.

15.5.3.5 Incident reports are to be prepared, in case of failures.

15.5.3.6 Trouble shooting & control measures to be adopted in case of emergency failures immediately.

15.5.4 Master Plan:

Master Validation Plan:

This is the first document to be reviewed by during inspection by a regulatory or control authority.

- It is a formal policy document which describes the overall philosophy of the company towards validation and which also describes the key elements of the validation programme, organizational structure of validation, schedules and responsibilities. It should describe: “Why, what, where, by whom, how and when?”

- The VMP should direct to the more specific, detailed documents such as protocols, reports and documentation preparation and their control, SOPs, and personnel training records.
- The VMP should identify which systems; facilities, equipment and processes are subject to validation, the nature and extent of such testing and the applicable validation and qualification protocols and procedures.

15.5.5 Maintenance & Calibration Procedures:

15.5.5.1 Request from the operating department for the service required (e.g. Maintenance, Calibration or qualification)

15.5.5.2 Identification of problem by maintenance / workshop department.

15.5.5.3 Start work on the rectification of problem.

15.5.5.4 Prepare the trial reports & records them.

15.5.5.5 Enumeration of the suggestions (if any).

15.5.5.6 Direction for handling, cleaning & lubrications of equipments.

15.5.6 Troubleshooting / Control Measures:

15.5.6.1 Examine the equipment & pinpoint the defect.

15.5.6.2 Check for any abnormal sounds or smells e.g.(burning).

15.5.6.3 Check for error messages.

15.5.6.4 Estimation of approximate time, when the fault could have occurred.

15.5.6.5 Try to identify the cause of problem (e.g. burning by high voltage /Temp shoot up.

15.5.6.6 Check the incident report (if any).

15.5.6.7 Inform the supplying company with details of equipment like make, design, model, Batch No., date of Mfg., Sl. No. , Purchasing date.

15.5.6.8 Fill up the service report.

15.5.6. 9 Purchase the materials required.

15.5.6.10 Rectify the problem.

15.5.6.11 Perform all performance checks, once the equipment is repaired.

15.6 Measurement Traceability

15.6.1 Policy

Standards and test equipment significantly affecting the test results conducted by the laboratory are monitored for stability as part of the measurement control program. Standards and equipment are calibrated and/or verified before use to ensure the recall or removal from service of any equipment or standards that are unreliable or that have exceeded the calibration interval if established.

15.6.2 Specific Requirements

15.6.2.1 To provide external evidence of traceability, the laboratory participates in proficiency tests, and other inter laboratory and collaborative experiments

15.6.2.2 Standards (Verification)

15.6.2.3 Continuous verification of standards, through testing on regular intervals and regular trend analysis ensures reproducibility of test and includes:

- Statistical data from standards and/or control charts and
- Results from inter laboratory comparisons and/or proficiency tests

15.6.2.5 Each item of equipment is labeled, marked, or otherwise identified to indicate its calibration status. All equipment used with nominal values and corrections is labeled indicating the calibration status. Examples of this equipment include thermometers, incubators and balances.

15.6.2.6 Calibration of equipment is conducted at a frequency to ensure that the equipment remains in tolerance during its use in the laboratory. Frequency of calibration is based on a review of calibration, maintenance, and repair history.

15.6.3 Reference Standards and Reference Materials:

15.6.3.1 Reference standards are calibrated against International Standards and are used regularly in all assays.

15.6.3.2 All reference standards are handled safely and stored in prescribed conditions to protect their potency and integrity.

15.7 Sampling:

15.7.1 Sampling plan for submitting samples to laboratory is dependent on the source of sampling.

15.7.2 In the case of vaccines to be used for Expanded Programme on Immunization for Government of Bangladesh, the samples from the finished final product are drawn by the respective officers of Ministry of Health and Family Welfare designated for the purpose. Onward transmission to lab is through courier services.

15.7.3 In the case of imported consignment, respective Drugs Control official of the port designated by DGDA of Bangladesh draw the samples and send it to laboratory through courier services.

15.7.4 Survey samples of Vaccine & biological are drawn by Drug Inspector of DGDA as per rules and are referred to lab for complete analysis.

15.7.5 Legal samples are also referred by Drugs Administration authorities, judiciary or police for opinion.

15.7.6 Samples for cold chain monitoring from field are referred by Drug Inspector of DGDA

15.7.7 Samples are also drawn by manufacturers and referred to lab for trade.

15.7.8 Samples once received in the lab are allotted a laboratory identification No. and stored in prescribed conditions handling testing. For testing, samples are picked up randomly and all tails of samples are entered in the relevant testing protocol or register as the case may be.

15.8 Handling of test and calibration items

15.8.1 Samples received for test are recorded in a laboratory work log and assigned a number which uniquely identifies the item during its stay in the laboratory. Work logs are maintained in the laboratory. A receipt is completed which includes: the sample or samples received for test, name of company submitting the test samples, and date of receipt. Study orders are taken on the receipt Performa.

15.8.2 Incoming test samples are stored under prescribed conditions as specified in **SOP no.NCL-GPL-018** by appropriate laboratory staff to ensure proper storage of the samples.

15.8.3 Prior to testing incoming samples, the laboratory communicates to the manufacturer any significant abnormalities including:

15.8.4 Departures from required standard transportation conditions and necessary preparations;

15.8.5 Doubt as to the item's suitability for test;

15.8.6 Nonconformance of the test sample with the description provided on the label; and Unspecified test requirements.

15.8.7 The laboratory handles, prepares, and stores test items in its custody in a safe manner to protect them from loss, deterioration, damage, and destruction of required chains of evidence. Documented procedures for the receipt and retention of the test samples are maintained in the laboratory files

15.8.8 Upon completion of testing, the test samples are safely retained for any feed back in future.

15.9 Assuring the Quality of test and calibration results:

15.9.1 The testing laboratory has a system for monitoring the validity of tests undertaken. The resulting data is recorded in a way that trends are detectable, where practicable, statistical techniques are applied to the reviewing of results. The monitoring shall be planned and reviewed and may include the following:

15.9.1.1 Regular use of reference standards to check the validity of assay.

15.9.1.2 Participation in inter laboratory comparisons or proficiency testing programme.

15.9.1.3 Assay Validations.

15.9.1.4 Correlation of results for different characteristics of an item e.g. trend analysis of testing results and reference standard. Comparison of results with that of manufacturer's results.

15.10 **Reporting the results**

15.10.1 Test reports are issued as per **SOP no----------** meant for reporting of samples received for testing under different categories.

15.10.2 General:

15.10.2.1 The unit in charge looking after a particular case shall examine the documents, shall prepare check list and summary sheet by thorough scrutiny and review of documents, ensure the testing as per study orders of unit-in Charge or Assistant Director, collects all reports from different analysts, cross examines them, get approved by unit-in-charge on all analytical reports, prepares draft reports on prescribed Performa and submit to U-i-C for approval.

15.10.2.2 The Officer- in-Charge shall approve the reports after complete review against raw data and order for typing and reporting.

15.10.2.3 A NCL control dispatch no. shall be issued on eachreport and necessary endorsement shall be made. Required no. of photocopies shall be made and checked by Unit-in-Charge. The office copy shall be signed by Unit-in-Charge and Officer-in-Charge.

15.10.2.4 After thorough review of each report, Officer-in-Charge shall forward the report to Deputy Chief of department for final authorization. The Deputy Chief shall authorize the report by signature seal (in some legal cases) and date of issue. In the absence of Deputy Chief, Officer-in-Charge or Govt. Analyst/----- discharges these functions.

15.10.3 Format of reports:

15.10.3.1 All reports shall be issued on authorized letter Deputy Chief.

15.10.3.2 All reports shall be addressed to the sample sender. Indicating subject, batch no. of the product, manufacturing date, expiry date, name of manufacturer, presentation and status (i.e. standard or not of standard quality) along with parameters of lot release (i.e. scrutiny of protocols, testing) followed by NCL no.

15.10.3.3 Copy of the report shall always be endorsed to DGDA of Bangladesh.

15.10.3.4 The report shall be dispatched under registered cover by postal services and by Fax to sample sender.

15.10.3.5 The office copies after dispatch shall be marked and signed by Dispatch-in-Charge and finally be attached with the case.

15.10.4 Opinion and interpretations:

15.10.4.1 In some cases, as per legal requirements, when reporting on Form 13, details of results or analysis with protocols of test applied has it be specified. A statement has to be given that the sample is of standard or is not of standard quality as defined in the Drugs Act,1940 and rules there under.

15.10.5 Amendments to test reports and calibration certificate:

15.10.5.1 Amendment to a test report after issue shall be make only in the form of a new report, which includes the statement: That previous report No. …….. dt. ……. may be treated as cancelled.

15.10.5.2 New report shall be uniquely identified and shall contain a reference to the original that it replaces.

16. Site Security

16.1 The laboratory is located within facilities of the Institute of Public Health. Security of the facilities is the responsibility of the Administrative Officer, Care Taker, and security guards. The Deputy Chief and Officer-in-Charge is responsible for security directly related to the laboratory and designates the specific duties of on-site security to the laboratory staff. Security of the laboratory premises includes the following:

16.1.1 Locking laboratory doors, in specific areas, when not in use;

16.1.2 Securing all doors and perimeter at the close of the day;

16.1.3 Notifying building security of disturbances and suspicious activity as appropriate;

16.1.4 Securing entrances to laboratory when disturbance during testing affects the test results; and

16.1.5 Securing all areas where standards and equipment are stored or maintained.

16.2 Access

16.2.1 Access to and use of all areas is controlled. List of the staff (laboratory or support) that has access to the specific area is maintained.

16.2.2 Laboratory main door keys are sealed, signed and given to security staff on duty. Time of depositing the keys with security staff is made in the register kept for this purpose. Individual room keys are kept in the locker in laboratory. A set of duplicate keys is duly sealed in the presence of security officer and kept with administration for use only in emergency.

16.2.3 Cleaning staff are only allowed supervised access to the laboratory during normal working hours.

17. Safety

17.1 Safe working conditions are prerequisite to good laboratory practices. Laboratory personnel are instructed in safe working practices and are encouraged to look for hazardous conditions as well as recommend and implement accident prevention.

17.2 The laboratory maintains a safety manual. The safety manual is available to all laboratory staff and management and contains all safety regulations associated with the overall laboratory operations

17.3 Safety Officer/Administrative officer is responsible Laboratory safety.

17.4 Management provides safe working conditions, complies with safety regulations and, along with supervisors, assures that the staff comply with these regulations.

17.5 It is the responsibility of all staff to be familiar with and comply with all safety guidelines and requirements. The laboratory staff takes proper precautions in the laboratory as described in the safety manual.

17.6 List of all hazardous and non - hazardous material is maintained.

17.7 All bio-hazard signs are displayed at appropriate places.

18. THE ANIMAL HOUSE

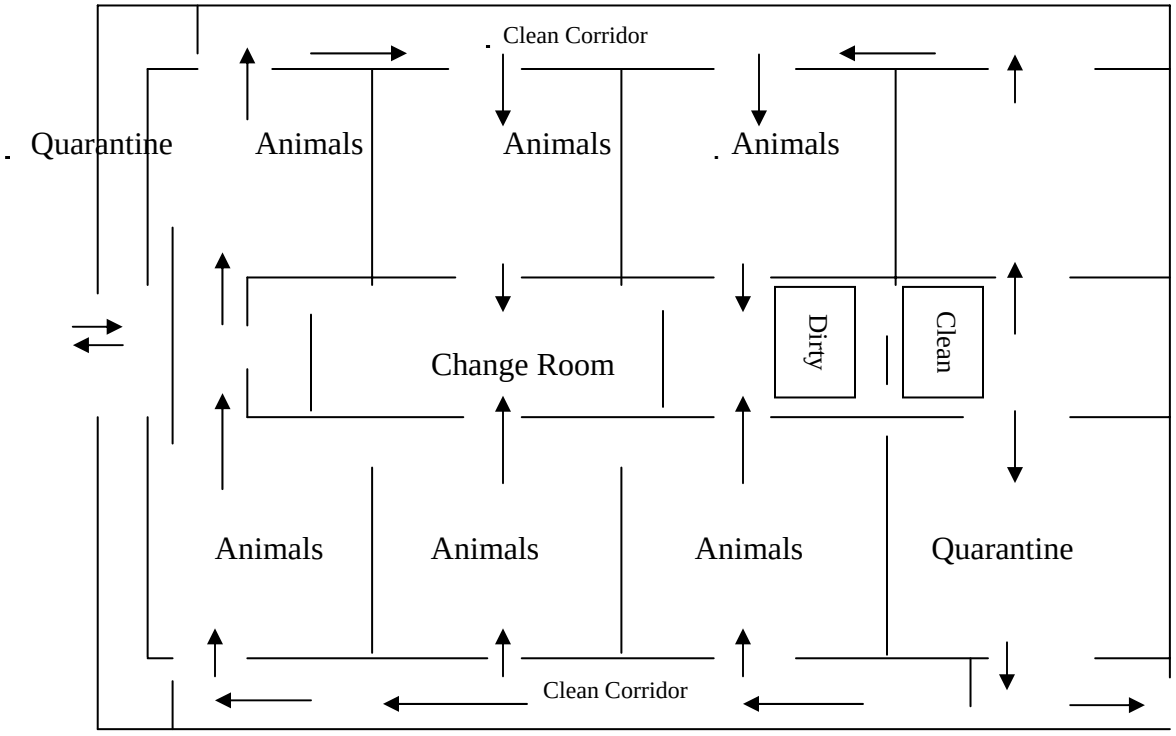


Figure: 2 An Ideal Animal House

Environmental variations have a specific impact on the mental and physical health conditions of animals, thereby results in a misleading outcome of the study. This variation may occur in both the macro and micro environmental conditions, which should be controlled. Environments of an animal house should permit the following:

- Most of the laboratory animals like rabbits, guinea pigs and mouse can tolerate a relative humidity of 40-70% and a temperature range of about 19^{o} to 26^{o} C. Normally this should be maintained or may be adjusted according to the animal we want to use.

- A thermograph for recording temperature variations and a hygrometer for moisture variation should be installed.
- Air of the animal house exchanged with fresh air free from any particulate matter at least 10-15 times an hour depending on the number of species and animals housed.
- Ammonia control is very important, as the ammonia is the metabolic product of urea in excreted urine of the animals by bacterial contamination. Room should be well ventilated and the beading materials of the cages should be changed accordingly.
- Laminar airflow system combined with HEPA filter reduces the airborne infections on laboratory animals.
- An adequate pre-HEPA filter can be installed to remove dust and hair produced by the caged animals with 12-hour light and dark cycling system.
- Noise leveling the animal area should be kept minimum level. Other wise at stressed condition of high noise level may cause enlargement of adrenal gland, reduce fertility, increased blood pressure, auditory damage and behavioral disorders.
- Walls and floors must be free from cracks and crevices, pipelines, drains and air filters should be well sealed to inhibit vermin to enter.
- Sticky traps may be placed in animal, feeding and service rooms to determine the entry of roaches and insects. The required measures can be taken to control their entry into the animal house.

- Physical separation of animals by species ensures the prevention of interspecies transmission of disease. All animals should be regularly observed for signs of illness, injury or abnormal behavior.
- Unexpected deaths and signs of illness, distress or other deviation formal animals should be recorded. Serological testing, bacterial culture, histopathology and DNA analysis by PCR may be used in combination to detect types of infections occurred.
- Euthanasia may be carried out in a manner that avoids animals' distress or in absence of other animals. Each animal room should have an entry and an exit door. The entrance door leads from the clean corridor to the animal room and the exit door leads the dirty things to an exit dirty corridor.

3.1. Animal Care and Use Protocols: The following topics should be considered in the preparation and review of animal care and use protocols:

Rationale and purpose of the proposed use of animals.

- Justification of the species and number of animals requested. Whenever possible, the number of animals requested should be justified statistically.
- Availability or appropriateness of the use of less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation
- Adequacy of training and experience of personnel in the procedures used.
- Unusual housing and husbandry requirements.

- Appropriate sedation, analgesia, and anesthesia could be applied and unnecessary duplication of experiments should be avoided.
- Conduct of multiple major operative procedures.
- Criteria and process for timely intervention, removal of animals from a study, or stressful outcomes are anticipated.
- Post procedure care should be ensured..
- Method of euthanasia or disposition of animal.
- Safety of working environment for personnel.

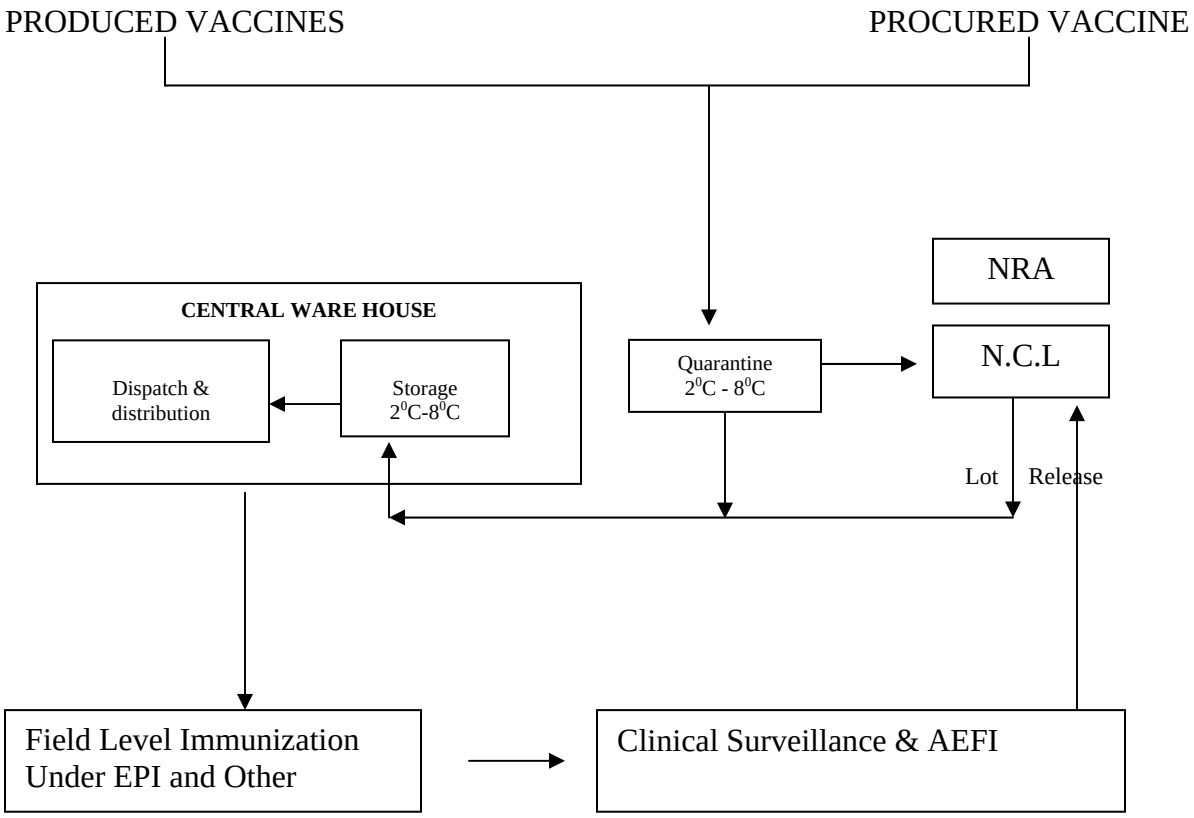
19. REVISION HISTORY

REVISION HISTORY			
Revision	**Description of Change**	**Approved by/Date**	**Effective Date**

20. REFERENCE DOCUMENTS

Annex No.8 of the Technical Report Series No.902 WHO

LOT RELEASE OF PRODUCED AND PROCURED VACCINES



Government of the People's Republic of Bangladesh
National Control Laboratory
Directorate General of Drug Administration
Ministry of Health & Family Welfare
Mohakhali, Dhaka-1212

Certificate number: NCL/ **Issue Date:**

To

Please refer to your letter no. ---------- dated : ---------- received in this office this is to certify that the following lots of ---------- produced by ----------, Dhaka in Bangladesh, whose lot numbers appear on the labels of the final containers, meet National and WHO summary protocol requirement(s).

Lot No.	Manufacturing Date	Expiry Date

As a minimum, this certificate is on the basis of test results from WHO affiliated laboratory of Thailand and examination of the Summary Protocol which includes the following information:

• Name and aDCress of manufacturer : ----------

• Site(s) of manufacturing : ----------

• Trade name and/common name of product : ----------

• Marketing authorization number : ----------

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

• Type of container : ----------

• Number of doses per container : ----------

• Number of containers/lot size :----------

• Date of start of period of validity (e.g. manufacturing date) and/or expiry date;

Mfg Date : ---------- Expiry Date : ----------

• Storage condition : ----------

A. A. Salim Barami
Deputy Chief (Deputy Chief of the Laboratory)
National Control Laboratory (NCL)

ORGANOGRAM OF NATIONAL CONTROL LABORATORY

Ministry of Health and Family Welfare (MOH&FW)

↓

Directorate General of Drug Administration (DGDA)

↓

A.A.Salim Barami
Director (Laboratory)

Deputy Chief (vaccine wing) | **Deputy Chief (Drug wing)**

Bacteriology unit	Virology unit	Pharmacology unit	Chemical unit	Engineering Dept.
1.Dr Nasima Pervin (Bacteriologist) 2. Md Hafizur Rahman (Asst. Bacteriologist) 3. Md.Riaz Hossain (Medical Technologist) 4.Md. Nazrul Islam (Medical Technologist) 5. Md. Abul Khayer Patowary (Lab. Attendant cum autoclave operator)	1. Miss Gouri Rani Bashak (Drug Super) attached 2. Md. Zabed Jahangir (Medical Technologist) 3.Mrs.Samsun Nahar (Medical Technologist) 4.Md. Hasmot Ali Mollah (Bottle Washer) 5. Dipu Kumar Kural (Sweeper)	1. Dr.Md Harun-Or-Rashid (Asst.Chief, Pharmacology) 2. Mrs Kamrunnahar Babli (Asst. Pharmacologist) 3. Miss Mahmuda Akhter (Medical Technologist) 4.Mr. Anowar Hossain (Medical Technologist) 5. Nannu Miah Patowary (Lab. Attendant cum autoclave operator)	1.Mrs.Syeda Sajeda Akter (Bio-chemist) 2.Md. Alauddin (Asst. chemist) 3.Mr. Mainul Hossain (Medical Technologist) 4. Md Abdul Hamid (Medical Technologist) 5. Md Habibur Rahman Chaklader (Lab. Attendant)	1. Md Mizanur Rahman Shah (SubAsst. Engineer, Electrical) 2.SubAsstt.Engineer- from IPH 3.Electrician / Instruments Mechanics - outsourcing 3.MLSS -- outsourcing