GOEL INSTITUTE OF PHARMACY AND SCIENCES, LUCKNOW

SESSION - 2022-23

SUBJECT - INDUSTRIAL PHARMACY - II

(BP702T)

An Assignment On

* OUT OF SPECIFICATIONS (OOS)
* ISO 9000 & ISO 14000
* GOOD LABORATORY PRACTICES
* NABL

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OUT OF SPECIFICATIONS

- The term Out of Specification (OOS) is used for those results of in-process or finished product testing which are falling out of the specified limits mentioned in compendia, drug master file, or drug application. The OOS may occur due to deviations in product manufacturing process, error in testing procedure, or faulty analytical equipment. A root cause analysis should be performed for investigating the cause of OOS.

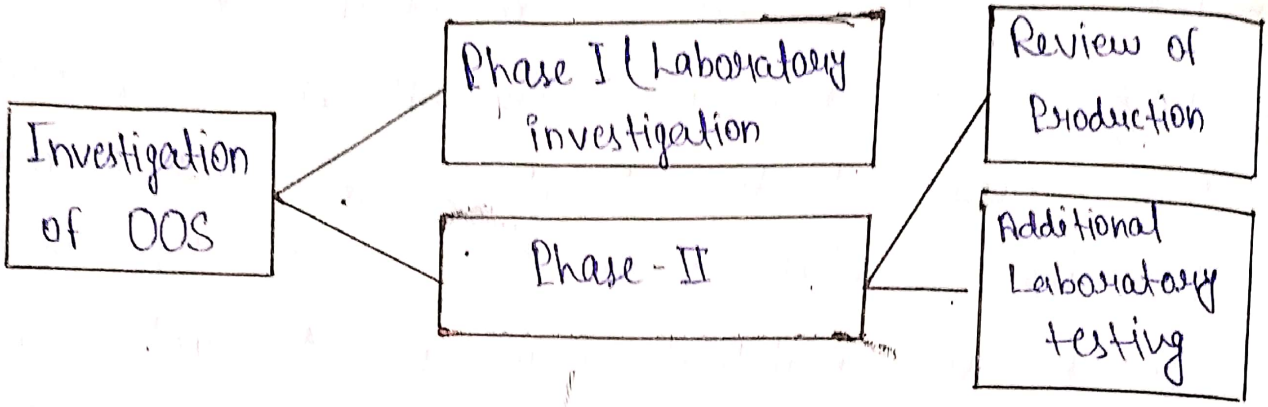
- The reason for OOS can be grouped as Assignable and non-Assignable.

- If the limits are not within specified range, it is called out of specifications. In case OOS has occured, the analyst should inform the QC manager. Then the senior manager should ask the QA for issuing OOS form to analyst.

- The responsible personnel should group the OOS as either assignable cause or non-assignable cause. Each OOS is given a unique identification number e.g: OOS/RM-001/2014.

Where, OOS - Out of Specification, RM - Raw Material (department), 001 - OOS for that year and 2014 - Year

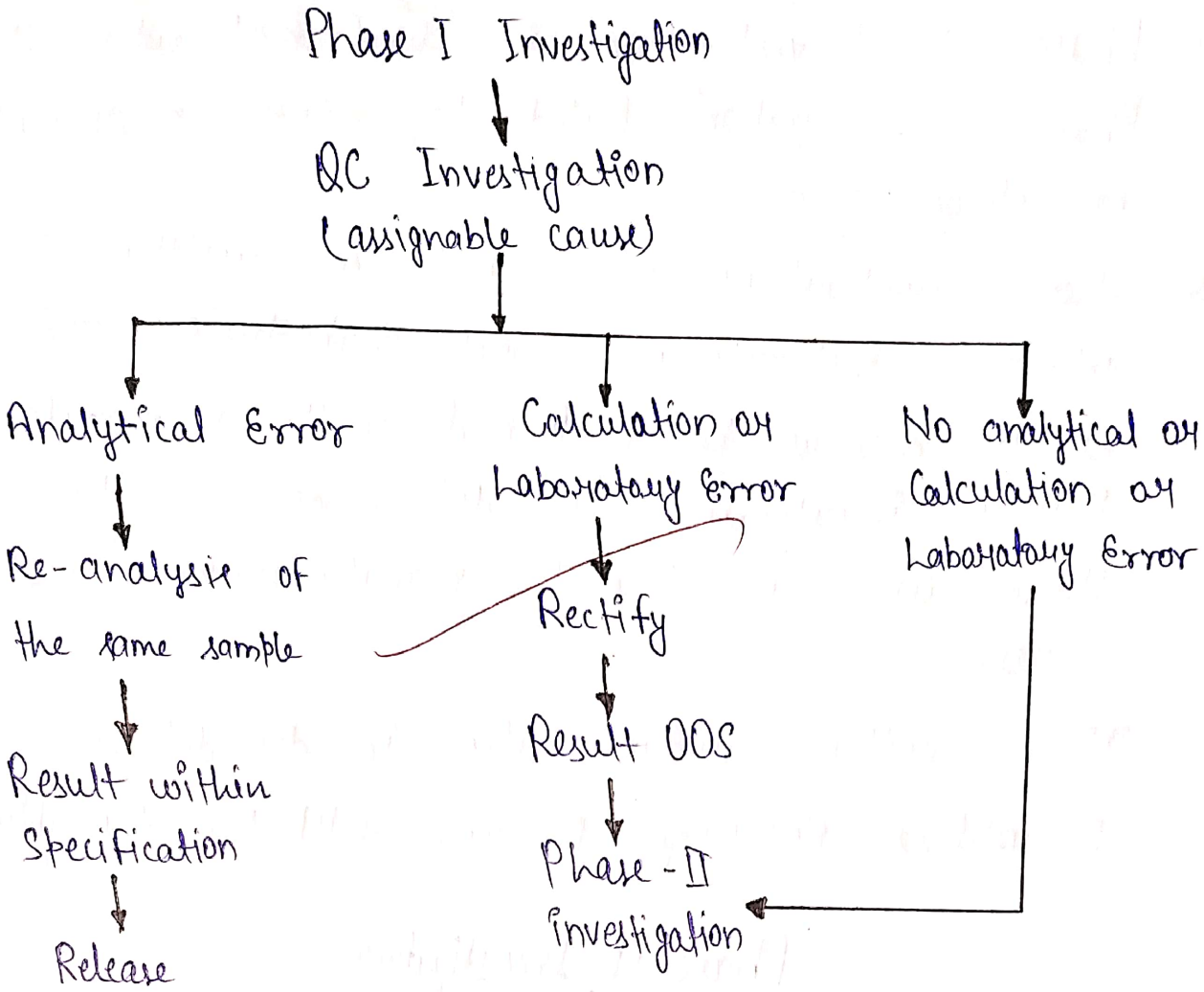
The OOS investigation involves two phases:



Investigation of OOS Results

Phase I (or Laboratory) Investigation

- Laboratory investigation is mainly performed to identify the reasons due to which OOS occurs.
- The reasons may include defect in measurement process or in manufacturing process.
- Regardless of the rejection of batches, the result obtained from OOS should investigate for their trend.
- The investigation should be performed for those batches that are resulted in OOS, or also to other batches and other products associated with OOS.



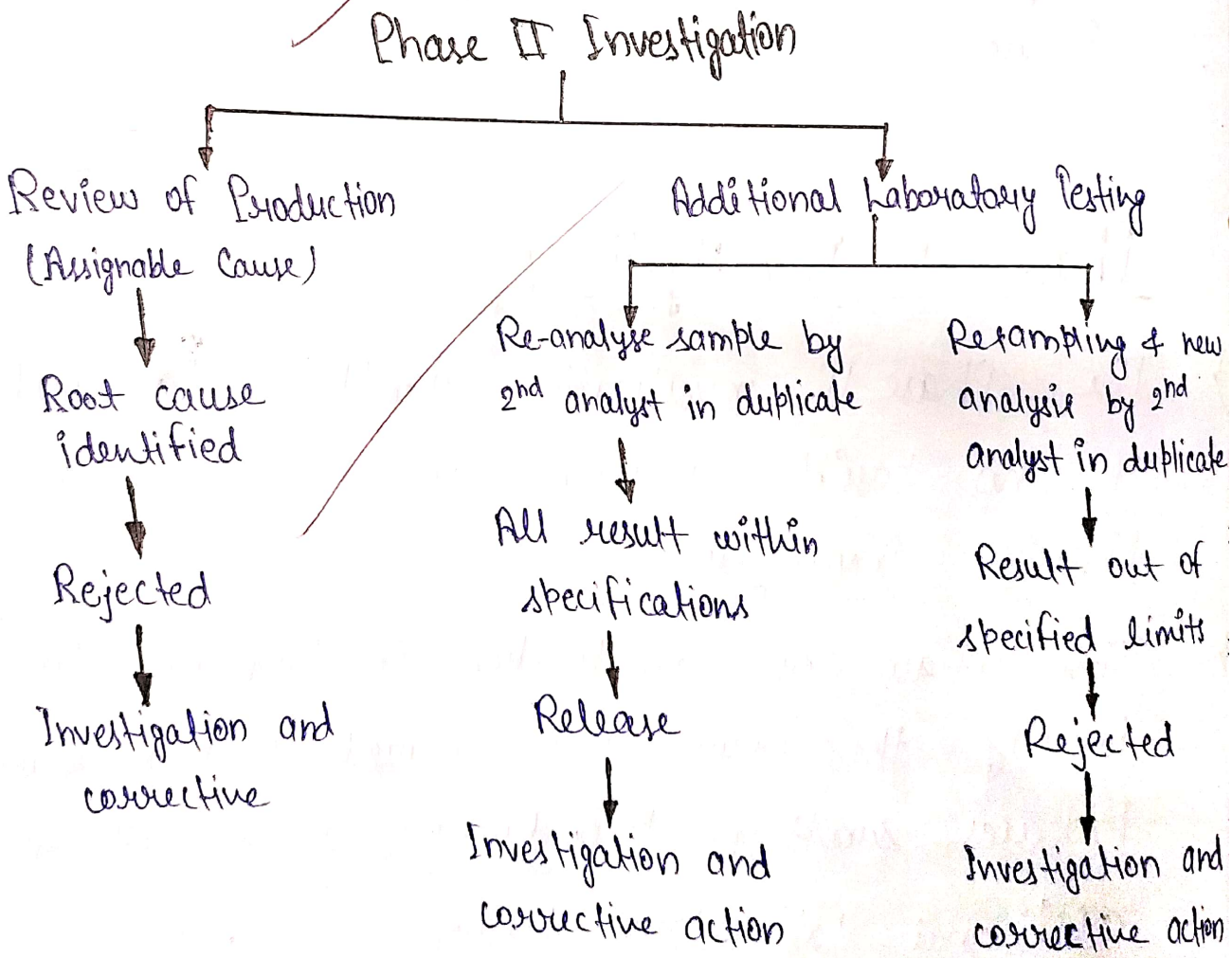
Phase – II Investigation:

- The Phase II investigation should be performed if no possible outcome is obtained from Phase I investigation.
- This phase of investigation is performed to identify the error that occured in manufacturing processes, sampling procedures, along with other additional laboratory testing.

⇒ Phase - II investigation is performed when the Phase - I investigation failed to expose an assignable laboratory error.

⇒ These investigations are based on written & approved instructions against hypothesis and should always be performed with a manufacturing investigation to determine whether there was a possible manufacturing root cause.

⇒ The written guidance also includes details on Resampling, Retesting, Averaging & Written description.



ISO 9000

ISO 9000 is a set of International Standards on quality management and quality assurance.

It has been developed to help the companies in effectively documenting the quality system elements to be implemented so that an efficient quality system can be maintained.

They are not specific to any one industry and can be applied to any, big or small organisation.

ISO 9000 helps a company to satisfy his customers, meet regulatory requirements, and achieve constant improvement. However, it is only considered as the first step as the base level of a quality system, and not a complete guarantee of quality.

ISO 9000 is widely recognised in the world.

It aims to implant a quality management system in an organisation for increasing productivity, reducing unnecessary waste, and ensuring quality of processes and products

Principles

There are the eight principles of ISO 9000 series:

1.) Customer Focus:
2.) Good Leadership
3.) Involvement of People
4.) Process Approach to Quality Management
5.) Management System Approach
6.) Continual Improvement
7.) Factual Approach to Decision Making
8.) Supplier Relationships

Working

- ISO 9000 is a collection of guidlines to help a company in establishing, maintaining, and improving a quality management system.
- ISO 9000 is not a rigid set of requirements, and organisations have the flexibility of implementing the quality management system in their own effective way.

This freedom enables various organisations and large and small businesses to use the ISO 9000 standard.

- ISO 9000 is process-oriented

Need for Obtaining ISO 9000 Certification

The software development organisations are in competition with each other to obtain ISO certification due to the benefits it offers.

Some of these benefits ~~are~~ that an organisation acquires by obtaining ISO certification are:

1.) The organisation gains customers confidence when it gets ISO certified.

2.) ISO 9000 requires a well-documented software production process that contributes to repeatable and higher quality of the developed software.

3.) ISO 9000 makes the development process focused, efficient, and cost effective.

4.) ISO 9000 certification recognises the weakness of an organisation and recommends corrective measures.

Importance

The importance of ISO 9000 is the importance of quality. Many companies offers product and services, but those efficiently delivering the best products and services are succesful.

Different bussinesses and even the customers recognise the importance of ISO 9000 and quality. And since consumer is most important to a company, ISO 9000 focuses on the customer.

Standards and Guidelines of

Standards & Guidelines	Purposes
ISO 0402 : Quality Management and quality assurance — Vocabulary.	Defines the fundamental terms used in the ISO 9000 family, which should be known to avoid internal & external misunderstandings.
ISO 9000-1 : Quality management and quality assurance standards— Part 1 : Guideline for selection and use.	Establishes a starting point for understanding and selecting the standards appropriate to needs.
ISO 9000-2 : Quality management and quality assurance standards- Part 2 : Generic guidelines for the application of ISO 9001, ISO 9002 & ISO 9003.	Assist in interpretation and application of ISO 9001, ISO 9002 and ISO 9003.
ISO 9001 : Quality system-Model for quality assurance in design, development, production, installation and servicing.	The requirement standard used to demonstrate capability for design/development of the product or services, and also for production, installation and servicing.
ISO 9002 : Quality system-Model for quality assurance in production, installation and servicing.	The requirement standard used to demonstrate capability for production installation, and servicing (identical ISO 9001 except for design control requirement).
ISO 9003 : Quality system-Model for quality assurance in final inspection and test.	The requirement standard used to demonstrate capability to control the product or service by final inspection and test.

ISO 14000

* The ISO 14000 family of standard provide practical tools for different companies and organisations who desire to manage their environmental responsibilities.
* ISO 14001:2015 and its supporting standards, such as ISO 14006:2011, focus on environmental system to achieve this.
* The other standards of ISO 14000 focus on audits, communications, labelling, life cycle analysis and environmental challenges, such as- climate change.
* The ISO 14000 family of standards is developed by ISO Technical Committee (ISO/TC) and its various sub-committees.

History

* Since 1947, the ISO has been developing voluntary technical standards for all sectors of businesses, industry and technology. The majority of ISO standards are highly specific to a particular product, material or process.
* ISO 14000 is different from most of the other ISO standards.
* Management system indicates the actions taken by an organisation to manage its processes or activities.
* The first standard, i.e. ISO 14004 and ISO 14001, were published in 1996 in the month of September and October, respectively.

Standards

ISO 14000 includes several standards under which the aspects of managing the practices within facilities, the immediate environment around facilities, and the product life cycle are covered.

Here are the key standards included in ISO 14000:

1.) ISO 14001 : Specification of Environmental Management System.

2.) ISO 14004 : Guideline Standards.

3.) ISO 14010 - ISO 14015 : Environmental Auditing and Related Activities.

4.) ISO 14020 - ISO 14024 : Environmental Labelling

5.) ISO 14031 - ISO 14032 : Environmental Performance Evaluation

6.) ISO 14040 - ISO 14043 : Life Cycle Assesment

7.) ISO 14050 : Terms and Definitions

Certification

* ISO 14000 Certification is achieved either when a qualified auditor verifies that all the requirements have been fulfilled or when a company self-declares so.
* Obtaining ISO certification is considered as a sign of commitment to the environment, which can be used as a marketing tool for companies.

* Other benefits of certification are that the company is permitted to sell products to other companies using ISO 14000 certified suppliers.

* Companies and customers also pay more for environmental friendly products. If the ISO 14000 standards are met, the product cost is reduced, as it encourages the efficient use of resources and waste limitation.

Benefits of ISO 14000 Certification

* There are various benefits of obtaining ISO certification. If a company adheres to the ISO 14000 standards, it results in better conformance to environmental regulations, greater market ability, better use of resources, higher quality goods and services, increased safety levels, improved image, and increase profits.

* Certification results in a wider market for goods and services of a company. Many corporations & governments look for ISO 14000 certified suppliers to maintain their own certification and reputation of environment friendly in market.

If ISO 14000 become successful, the already ISO 14000 certified companies will have an advantage in global markets. The producers of consumer goods will realise that many consumers purchase goods from environmental friendly companies.

GOOD LABORATORY PRACTICES

Good Laboratory Practices (GLP) is a set of principles that ensure the quality and integrity of non-clinical laboratory studies designed to support research or marketing of products regulated by government agencies.

The term GLP is associated with the Pharmaceutical industry and the required non-clinical animal testing to be performed before approval of new drug products. However, GLP term applies to many other non-pharmaceutical agents also such as colour additives, food additives, food contamination limits, food packaging, and medical devices.

New Zealand and Denmark are the countries where GLP was first introduced in 1972.

GLP was instituted in US after the fraud cases generated by toxicology labs in data submitted by pharmaceutical companies to the FDA.

General Provisions

The GLP regulations set out rules for good practices and assist the researchers to work in compliance with their own pre-established plans and standard procedures. The regulations neither include the scientific or technical content of the research programmes, nor evaluate the scientific value of the studies.

All GLP texts, regardless of their origin, state the importance of the following:

1.) **Resources:** Organisation, Personnel, facilities & Equipment.
2.) **Characterisation:** Test items and test systems.
3.) **Rules:** Study plans (or protocals) & written procedures.
4.) **Results:** Raw data, final Report and Archives.
5.) **Quality Assurance.**

* The major points to be considered under GLP are given below:

1) The Laboratory should be located, designed, customized, and maintained to suit the performance of all quality control tests and analyses.
2) There should be seperate wings for analytical, instruments, microbiology, sterility, etc. which should be connected with the internal door.
3) There should be an effective airlock, provisions for A.C. and fumigation chamber. The laboratory should have adequate space.
4) The laboratory furniture should provide adaptability. The table top should be covered with material that is resistant to acids, alkali, solvents etc.
5) The floor should be smooth, easy to clean and should have adequate drainage facility.

Equipments

* There should be a written SOP for each instrument. The instruments should be located in a seperate room under controlled temperature.
* They should be handled with care and should be kept clean.
* The surrounding area should also be cleaned.
* The calibration and maintenance / service record should be done periodically.
* The glassware should be caliberated prior to use.

Chemicals and Reagents

* Storage of chemicals and reagents should be done adequately under recommended storage conditions.
* The container of all chemicals and reagents should be properly labelled.
* Chemicals should be transferred with utmost care.

Documentation

Document is a critical factor of the GLP as documentation involves recording information for future references.

The major documents that should be provided are protocals, logbook for usage, etc. Well-established SOPs should be provided for the maintenance and calibration of equipments.

Some common information routinely recorded in a laboratory are given below:

1) Receipt and storage of sambles
2) Sampling
3) Analytical testing
4) Validation
5) Calibration
6) Data Recording
7) Operation of instruments
8) Reagent preparation.
9) Training records
10) Organisational Charts
11) Sampling procedure
12) Analytical testing methodology
13) Inventory / list
14) Instrument calibration data
15) Methods validation data
16) Analytical testing results and reporting.

Quality control

* A well-defined procedure should be established, including all the aspects related to the sample, i.e, receipt of the consignment, sampling techniques to be adopted, storage and handling of samples, recording and reporting analysis.

Every received sample should have a unique number mentioned on the label.

Records and Reports

* The laboratories should maintained record of all the test performed.
* The graphs related to IR, HPLC etc. should also be stored along with the raw data.
* The access to records to an authorized person should be restricted, and these records should be stored under lock and key.

Safety

* Proper facilities and accessories should be provided for the safety of personnel involved in drug testing.
* Adequate anti-doses should be available for the accidents that may occur.
* Suitable equipment should be provided for extinguishing fire in case of accidental fires.

Auditing Procedure

The quality assurance department of a laboratory should establish a committee that need to regularly audit their facilities for ensuring compliance with GLP requirements.

NABL

* National Accreditation Board for Testing and Calibration Laboratories.
* NABL is a Constituent Board of Quality Council of India.
* Its goal is to provide Government, Industry Associations and Industry with a scheme of Conformity Assesment Body's accreditation that involves third party assesment of the technical competence of testing, including medical and calibration laboratories, proficiency testing providers, and reference material producer.
* NABL is an autonomous body under the Department of Science and Technology, Government of India, and registered under the Societies Act.

Benefits of NABL

1) Due to accreditation status, costomer confidence in testing and calibration reports issued by the laboratory has increased.
2) Due to enhanced customer confidence and satisfaction, the business of laboratory has also increased.
3) Accreditation provides better control over the laboratory operations.

4.) Laboratories get feedback about their technical capability and quality assurance system.

5.) Database or directory of NABL accrediated laboratories is made available both online & offline. Customer can easily access NABL accredited laboratories for their specific requirements.

6.) NABL accreditation results in time and money saving as the need for re-testing of the products is reduced or eliminated.

Scope of NABL Accreditation

NABL provides accreditation in the following fields and disciplines:

1) Testing Laboratories
2) Medical Laboratories
3) Calibration Laboratories
4) Proficiency Testing Providers
5) Reference Material Producers

The following fields related to the Pharmaceu
are covered under the scope of NABL Accreditati

1) Drug and Pharmaceuticals
2) Cosmetics and essential oils
3) Ayush products
4) Plant and Plant material
5) Cell culture

6) Molecular Analysis
7) Resistance to microbial attack
8) Toxicology
9) Veterinary Testing
10) Nutraceuticals

Procedures

Various steps to be followed in NABL accreditation process are discussed below:

1.) **Application for NABL Accreditation:**

* The laboratory that desires to get NABL accrediatation submits an application in prescribed form (NABL form 151 for testing laboratories; NABL form 153 for medical laboratories; NABL form 180 for proficiency testing providers and NABL form 190 for reference material producers) along with its quality manual and prescribed fees.

2.) **Acknowledgement of Application:**

* The NABL secretariat, on receiving the application in the prescribed formate, issues an acknowledgement and assigns a unique ID number to it.

3.) **Review by lead Assessor:**

* The NABL secretariat appoints a lead assessor to evaluate the application & quality manual, and

submit its report to NABL secretariat.
The lead assessor thoroughly review the quality manual submitted by the laboratory and if find any insufficiency, ask the laboratory to amend it.

4) **Pre-Assessment:**

* The lead assessor visit the laboratory for a pre-assessment of the degree of vigilance of the laboratory for evaluating any non-conformity in the implementation of the quality system and for determining the number of assessor(s), required, key location to be visited etc.

5) **Assessment:**

* NABL makes an assessment team, including the lead assessor technical assessor(s)/expert(s) and an observer, after consulting the laboratory that has applied for NABL accreditation.
* NABL then consult the laboratory & the assessment team to fix a dates for on-site assessment.

6) **Scrutiny of Assessment Report:**

* The NABL secretariat examines the assessment report. If any insufficiency is found in the report, the laboratory takes corrective actions as suggested by the assessment team.

7) Accreditation Committee:

* This committee examines the assessment reports and also the report the laboratory has submitted regarding the corrective action taken by it.

8.) Issue of Accreditation Certificate

* If the recommendation of the accreditation committee is positive, the laboratory is granted accreditation and is also issued an accreditation certificate by NABL.

* This Certificate bears a unique accreditation number, NABL hologram, date of validity, discpline and scope of accreditation.