Planning and Designing of a Toxicology Lab at AIIMS Bhopal

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ABSTRACT

Toxicology lab is the need of an hour to identify and confirm the presence of a toxic agent, chemical or poison inside the body. Both types of examination is possible in a toxicology Laboratory i.e. qualitative and quantitative for a toxic chemical or poison and in return helps in investigation of a medico-legal case or the necessary treatment and management with the follow up. Being a newer organisation, AIIMS Bhopal is set to develop a modern toxicology lab from its inception to a fully functional core lab for analysing those harmful substances in the body and will have shared facilities to provide sophisticated equipment and expertise to facilitate biomedical research across a range of disciplines including dissemination of information on poison and poisoning through a nodal poison and drug information centre.This study aims at to discuss the available literature and requirement for establishment and functioning of toxicology laboratory and to frame up a model which can serve as an reference in Indian scenario. The study also gives a brief idea of various logistics including manpower required for starting such a facility at AIIMS Bhopal and its working to some extent.

INTRODUCTION

Toxicology is the study of the effects of chemicals agents on living organisms. It is used to detect and analyze substances of abuse, drugs, alcohol and other poisons. The discipline of toxicology has undergone rapid streamline with the advancement of instruments. It is important to have standard and uniform guidelines and necessary accreditation for setting up a modern toxicology laboratory which in return provide timely, accurate and meaningful results[1,2,3]

Toxicology Lab as Core Lab

Core laboratory refers to the term of a (consolidated) diagnostic laboratory where shared facilities will be provided in terms sophisticated equipment and expertise to facilitate biomedical research across a range of disciplines on a single platform. They are designed to create economy of scale, less manpower involved and lower costs of quality control and assessment reagents etc.[4,5] At AIIMS Bhopal, the department of Forensic Medicine & Toxicology along with the dept of Pharmacology will develop the toxicology lab as core lab and it will function for:

1. Post-Mortem Forensic Toxicology
2. Clinical Toxicology
3. Animal Toxicity studies
4. Nodal Poison and Drug Information Centre

***Nodal Poison and Drug information Centre*:** In India, the National Poisons Information Centre (NPIC) was established in Feb, 1995 in the Department of Pharmacology at the AIIMS, New Delhi. The associated toxicology laboratory at AIIMS Bhopal will provide the necessary analytical services to the nodal Poison and Drug information Centre and It will be a step towards the poison control centre unit which not only provide information on prevention, early diagnosis and treatment of poisoning/drug toxicity and hazard management but at some extent assist in its detection of consumed agent. This information service will remain be available round the clock. [6,7,8]

Aims and Objectives of the Study: At present various models exist for establishment and functioning of toxicology laboratory and they are supposed to full fill the minimum basic requirement. In India where more and more AIIMS like Institutions are being established and it is difficult to start a toxicology lab starting from zero especially in the absence of guidelines. The study aims to review the various models available in the literature and to frame up a model which can serve as a reference for setting up of a toxicology lab in Indian scenario.

DISCUSSION

Despite considerable progress in analytical chemistry and clinical toxicology/poisons Information centres, execution of analytical toxicology services remains a challenging task. Bilateral services between the emergency dept and the regional /national public health centres can make the balance between the need of patient care and best use of available resources. Analytical services in emergency will normally be provided by hospitals clinical chemistry laboratories, while regional centres may be associated with clinical chemistry laboratories, with forensic services, with a poisons centre, or even independently operated. It should always be retained in mind, that any poisons analysis may have medico-legal implications hence the possible standard operating procedures for analysis in a laboratory must be the goal [9,10,11]

The Society of Forensic Toxicologists (SOFT) and American Academy of Forensic Sciences (AAFS) have published detailed guidelines on the smooth functioning of forensic toxicology laboratories, much of which is applicable to clinical toxicology laboratories (SOFT/AAFS, 2002). Laboratory operations can be divided into pre-analytical, analytical, and post-analytical phases.

The laboratory must have a standard operating procedure manual (SOP) that should be completed, up-to-date, and available to all persons who might be executing the analytical work. The SOP manual must include detailed descriptions of procedures for receiving of sample, quantity of sample, execution of laboratory procedure, chain-of-custody, quality control and quality assurance(including method development and method validation, calibration of instrument internally as well as externally, troubleshooting) review of data, and reporting of results.[11] A list of organisations from UK and Ireland have contributed for the establishment of UKIAFT Forensic Toxicology Laboratory guidelines.[12] The Detailed guidelines concerning forensic toxicology, clinical toxicology, point-of-care testing, and an area of coincidence of test results are provided. Guidelines and standards exist for forensic toxicological analysis used in general and specific situations, e.g. routine chemical examination in laboratory and point of care testing like driving under the influence of drugs and alcohol. For Post-mortem forensic toxicology and human performance forensic toxicology detailed guidelines exist in the proceedings of SOFT/AAFS/2006 which gives emphasis on the scope, personnel, and the other requirements including SOP's, guidelines for sample collection, preservation and storage, maintaining chain of custody with proper labelling, recommended amount of samples taken, safety measures to be taken for hazardous and carcinogenic chemicals which can affect human life and the environment. The guidelines also stressed upon the analytical procedures including screening and confirmatory tests, calibration and method validation procedures. The focus was also given on quality control and quality assurance, review of data and reporting of results. A part of these guidelines also mentioned interpretation of toxicology results and safety issues. The Post-mortem forensic toxicology and human performance forensic toxicology surrounds itself within the area of identification and quantitation of ethanol and other drugs, chemicals in blood and other appropriate biological samples excluding the breath ethanol analysis. Some governments include the methods for blood alcohol testing for persons driving under the influence of alcohol in their laws.[11] Guidelines in the area of clinical toxicology, not only focus on the analytical aspects of analysis but also on the promptness of results. According to the US- and UK-based practice guidelines for the emergency department, the turn-around time should be 1 or 2h, respectively, for a specific set of analysis. Guidelines are either being developed or already available for point-

of-care testing in analytical toxicology.[13] Apart from this there are many regulations, standard references, scope, building requirements, building design issues, laboratory design consideration, mechanical consideration, environmental control, hazardous material storage and bio safety level etc. need to be taken in to consideration for the establishment of a laboratory.[14]

While setting up the lab a prospective attitude with a practical approach is needed. The outcomes of the laboratory should be capable enough to serve the society even after years. This vision will not only help for the initial set up of the laboratory but also help in the future perspectives regarding NABL accreditation and smooth running of various research projects. A free software is available in the market for lab management and inventory that can use from the beginning to keep track of what you need for initial set up and the followed requirements.[15] To set up a new laboratory, evaluation of the space is very necessary to determine the requirements for processing of analytical test of materials. The records and results can be reproducible and retraceable with better and effective quality. A separate place and safety guidelines are needed to store and use of carcinogenic and hazardous chemicals and biological materials.[16]

Basic Steps in Setting up of a Toxicology lab[17,18,19]

Experts have probably written varied books on individual steps and based upon different models available. Some basic steps to be taken in to consideration are as follows:

Step 1: Selection of a Test Menu

Selection of the list of tests that the laboratory will offer affects all the remaining steps used in the process A common mistake made frequently during the set up a new laboratory is the trial to perform every analysis.In order to run the laboratory in a successful condition, one needs to have enough analytical methods and procedures that can be fit into the laboratory's financial budget.

Step 2: Location

Search for required physical space(Image I&II) for the laboratory depending upon various types of analytical tests intended to be performed in the laboratory. It should be kept in mind while selecting a space that a constant temperature and proper ventilation is required to run a laboratory successfully, and for that a reliable HVAC/controlled temperature environment system is must. Adequate plumbing for a sink and eyewash station is also the need of an hour in the laboratory. Flooring should be of any impenetrable material such as cement, tile or vinyl to avoid any fatal accident during the analysis which is most common and for that carpet and other materials that are proved to be of explosive nature should be avoided.

Step 3: Instrumentation

The necessary equipment along with the necessary accessories required for analysis need to be selected to perform the tests selected in the test menu. The concept of prudent buying (as GFR rules for procurement) shall be applied. Along with the purchase price other things like CMC, AMC, additional equipment accessories, spare parts and their warranty can be negotiated. The power supply sockets and the required quantity of power supply needs to be checked.The software and troubleshooting of the errors of the instrument needs to be discussed before buying. Place and supply of gases (Gas cylinder) needs to be checked if required for a particular instrument.

Step 4: Laboratory Information Management System (LIMS)

This system can be used by the staff for maintaining chain of custody for the samples, maintaining stock entry for the chemicals, consumables and other equipment and their accessories. The log books must be maintained for every instrument and each type of analysis individually Separate records regarding the installation of instruments, their internal and external calibrations, troubleshooting of the errors, quality control and quality assurance needs to be maintained The current movement in LIMS systems is to cloud-based models

Step 5: Revenue Cycle Management

The source of finances is the most important consideration. Money outflow for purchase of required consumables and a funding source for the inflow need to be determined and inflow and outflow must be in equilibrium.

Step 6: Staff Requirements

The most important assignment while staring a toxicology laboratory is the recruitment of well qualified and well trained staff The clinical laboratory being a highly regulated set up, the credentials and certifications of the staff personnel are very important. Each high complex

laboratory is required to have a lab –In charge, clinical consultant, scientific staff, technical staff and cleaning staff. One person can fill multiple roles, so it is especially important for small labs to follow strategy in recruitment process.Manpower(approximate as per the need of work) required:[20]

S.No	Name	No of persons
1	Toxicologist	02
2	Chemist	02
3	Technician	06
4	Laboratory Assistant	02
5	Laboratory Attendant	02
6	Security Guard	02
Total		16

Step 7: Accreditation[21]

Accreditation is the necessity where external services are provided. Accreditation can be done for a specific method of analysis or for all services provided by the laboratory. The process of accreditation is very tedious, takes time and it will be granted for a limited time period. IS/ISO/IEC17025:2017 will be applicable to Forensic /Clinical Toxicology Laboratories.

Design Guidelines [2,11,17,18,22]

1. Laboratory Air Flow: Every toxicology laboratory must have a bio vestibule unit which prevents the cross contamination of the laboratory air to the corridor. Entries and exits into the laboratory system must be done through the bio vestibule unit and the unit must have a attached sink with it.

2. Laboratory Space

The laboratory space is divided into two categories:

A) Wet Toxicology Unit: This unit plays a major role in sample collection, preservation and processing which includes Extraction of the required sample from the biological matrix followed by its isolation and preliminary Screening. The unit is advantageous as the sample cannot be analyzed directly on the instrument and it gives a direction to the analysis by preliminary screening thus in result reducing the cost and time of analysis.

The unit must be equipped with the following facilities:

i. Individual workstation for individual steps in sample processing.

ii. All glassware, reagents and chemicals required for analysis must be readily available.

iii. The laboratory should be well equipped with the minor equipments required for analysis.

iv. The laboratory must have a fume-hood system to deal with the experiments that involved the carcinogenic and acidic fumes. The fume-hood must have attached sink in it to process the risky samples. it also has bench top space with hood and sink as required for specific equipment and procedures.

v. The laboratory must have a evidence storage facility i.e. refrigerators with emergency power system.

vi. The Waste management system according to the biohazard waste management and Dry fire-suppression system must be present in the laboratory and all persons working inside must be aware about the guidelines and safety procedures about it.

vii. There should be a adequate space to maintain and handle data in soft copy as well as hard copy and electrical ports for computers and instruments

B) Instrumentation Unit:

Individual bench top space along with some extra space for sample handling, reference preparation, instrument maintenance, utility access with fume hood, solvent storage, and a separate sink is needed for each instrument separately.

Storage cabinets for reference materials and manuals should also be present separately for each instrument. Separate place is required for keeping the gas cylinders with safety which was used as an assembly for the instruments. The panels fitted for the same will be done with utmost care.

The power supply needed is different for each instrument and that should be taken into consideration. Also the cooling requirement varies with each instrument and that should be taken care of before analysis. Interruption because of these might result into instrument degradation.[22,23]

Space required for documentation and administrative

work

Space is required to keep the documents, sample graphs, calibration curves:

1. Record (external documents) keeping space to maintain chain of custody.
2. Individual workstation for each toxicologist for administrative works.
3. Space to keep internal documents like calibration graphs sample graphs etc for each instrument.
4. Space is required for sample receiving, sample storage and report giving along with the remaining leftover sample of the case.
5. Extra and separate space is required to keep the contagious and confidential samples
6. Separate space is also required to keep the fire and explosion safety items.

Standard Operating Procedures(SOPs) [21]

1. The laboratory must have standard operating procedures for every single and small process.
2. The standard operating procedure manual should be available to each and every individual working in the laboratory and involved in analytical work.
3. The standard operating procedure manual should be up to date, and completed in all respects.
4. Detailed instructions of procedures for sample receiving, their handling, storage, chain-of-custody, analysis, quality control and quality assurance, review of data, and reporting, safety precautions should be documented.
5. There should be a separate SOP for Administrative procedures as well as analytical procedures
6. Sample signatures and initials of all individuals handling specimens and performing analytical work should be present in the standard operating procedure manual("signature page")

Samples and receiving

Specimen Collection and Labelling: The proper selection of samples followed by their collection and preservation with proper labelling and then submission of specimens for toxicological analyses is of paramount importance

Specimen Handling: A Form mentioning details of chain-of-custody from the place of collection to the laboratory to provide with the specimens. The laboratory-request form for the particular analysis must be filled with all details of the samples to be analyzed. A proforma for sample received should also be filled and given to the person submitted the sample to the laboratory. The receiving laboratory must record the means of delivery of the samples. The quantity and quality of the samples along with the number of samples must be recorded

Security and chain-of-custody: Entry of unauthorized persons should be restricted inside forensic toxicology laboratory Entry of authorized persons should be made using the biometric system Unauthorized personnel entry if required then they should be escorted and required to sign a log-book upon entry and departure

Quality Control: Quality control in Forensic Toxicology is very narrow and limited as every case is different and unique in its own terms like type of sample, biological matrix, quantity consumed, weight and age of a person/

Budgeting [22]

Table A: Extraction and isolation unit

S. No.	Name	Estimated cost (Rs)
1	Glassware	400000
2	Tissue homogenizer	200000
3	Steam distillation unit	70000
4	Oven	400000
5	Water distillation unit	500000
6	Hot plate	10000
7	Microwave digester	1200000
8	Vortex mixer	40000
9	Desiccators	50000
10	Centrifuge machine	40000
11	Water bath	30000
12	Fume hood	500000
13	Electronic balance	70000
14	Top loading balance	30000
Total		35.4 Lakhs

Table B: Screening test unit[30]

S. No.	Name	Estimated cost (Rs)
1	Chemicals	1000000
2	Refrigerators	50000
3	Standard reference sample	1000000
4	pH meter	40000
5	Breath alcohol analyzer	200000
6	TLC preparation system	300000
7	U.V cabinet	200000
8	Kits for rapid screening of drugs	100000 for each kit
9	Conductivity meter	30000
Total		29.2 Lakhs

Table C: Sophisticated instrumental unit[30]

S. No.	Name	Estimated cost (Rs)
1	Gas Chromatography – Headspace(GC-HS)	4000000
2	High Performance Liquid Chromatography (HPLC)	2000000
2	Gas Chromatography – Mass Spectroscopy (GC-MS)	15000000
3	Liquid Chromatography – Mass Spectroscopy (LC-MS)	20000000
4	Inductive Coupled Plasma Atomic Emission Spectrom-etry	15000000
5	Fourier Transform Infra-red Spectroscopy	1500000
Total		5.75 Cr

deceased, stomach filled or empty, treatment taken or not, external circumstances etc. For forensic toxicology procedures, comparing with a true control is next to impossible. Calibration of all the instruments must be done prior use. Both internal and external calibration should be checked every day before sample analysis. Standards used in calibration must be obtained from tested and verified places. The test methods used in analysis must be validated before sample analysis

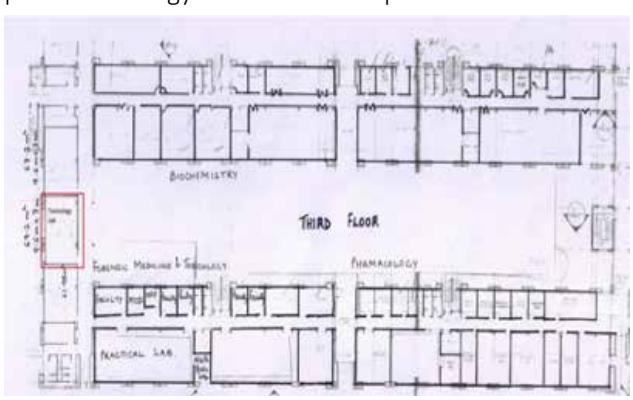
Quality Assurance:[24] Quality assurance is a major concern in Forensic Toxicology laboratory as the results obtained will be used to help criminal justice system. Quality assurance started from the sample collection followed by the analytical work and result and ended up with the data interpretation and report writing Quality assurance is the proficiency testing or random check of the methods and other equipments used to maintain the quality control procedures Internal and external audits should be done randomly for quality assurance

Reference Materials:[9,25] Forensic Toxicological analysis always involves the comparison with the standard reference materials. The standard reference materials should be having purity upto 99.99%. The standard reference materials should always be checked for any error before use The standard reference materials should be tested from time to time for their shelf life and quality

Review of data:[26,27] Before giving final report all the necessary and relevant information written in the report must be checked by the higher authorities The following points needs to be considered Proper documentation

Fig:1 Proposed toxicology lab at AIIMS Bhopal

Fig:3 Physical location in map and dimensions of proposed toxicology lab at AIIMS Bhopal



to maintain chain of custody Analytical procedure used and its validation details Calibration of equipments with quality assurance details Where possible, the results should be reviewed in the context of the case history, autopsy findings and any relevant clinical data.

Reporting of results:[28] Toxicology laboratories being an integral part of state government supports medico-legal investigation system. Each laboratory must follow the guidelines and reporting format of that particular state. It is not possible to suggest a uniform format for reports in the country but one should include all necessary information to identify the case and its source, test results and the signature of the individual. Confidentiality at each stage must be maintained.

Reporting:[29] There should be a procedure in the SOP manual for sending a report to the investigative system. Referred Tests -If samples are forwarded to another laboratory for analysis, then it should be mentioned in the final report. Retention of a copy of all the Records in the laboratory is mandatory Records should be retained as long as practical, but for at least 5 years. Records should include a copy of the report, request and custody forms, work sheets, laboratory data, test graphs, calibration curves, repeatability and reproducibility documents, quality control and proficiency testing records. Laboratories are strongly encouraged to record the data in digital form along with the paper records.

CONCLUSION

To Setting up of a toxicology lab needs meticulous planning, adequate space and manpower along with sufficient budgeting according to the work load. There should be laid down the standard operating procedure to ensure efficient and error free functioning of the lab at all the levels with the emphasis om quality assurance and quality control. This Toxicology lab at AIIMS Bhopal will be unique in having an integrated poison information centre to disseminate information and would work as core lab.

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