GOOD LABORATORY PRACTICES

1. Analysis should be carried out according to the documented procedures/ specifications. Analysts should not change documented methods unless the changes are duly authorized.

2. All observations and calculations should be recorded on the Analytical Report on the reverse side and conclusions on the front. Calculation sheet can be attached wherever possible. Reports can be generated with the use of computers in similar manner.

3. Wrong entries should be scored with a single line and the new entry made alongside with an initial of the person correcting the mistake. Pleases do not overwrite.

4. Every analysis should carry the date on which it was carried out. Spectra and other test records should be attached to the Analytical Report and filed in the docket.

5. All reagent bottles/chemicals should be properly labeled and stored in the identified areas or shelves.

6. Labels should indicate the date on which the reagents were opened/prepared or standardized.

7. Spoiled and disfigured labels should be replaced.

8. Labels which are not current should be peeled, covered with the no. label or crossed with ink, whenever a solution is changed or freshly standardized, solvent bottle should be kept in respective shelves after use.

9. Laboratory should be maintained in a clean and orderly manner at all times.

10. Care should be taken that instruments should be switched off and covered at the end of the day.

General Instructions:

1. Keep all gangways, exits and fire fighting equipment free from obstruction.

2. Do not smoke, eat or drink in the laboratory.

3. Ensure that all chemical waste is disposed off in a predetermined manner.

4. All injuries, no matter how slight, must be treated immediately.

5. Any accident, however slight, must be reported.

Volatile materials:

1. Volatile solvents and corrosive liquids should never be pipetted directly.

2. Do not pour out volatile solvent near a naked flame.

Reference: http://amitpatel745.topcities.com/index_files/study/glp.pdf

Corrosive Chemicals:

1. These should be prevented from coming in contact with body surfaces, including eliminatory and respiratory systems. While handling these, rubber gloves, rubber aprons, safety goggles and other necessary safety apparel must be worn.

2. Do not store large bottles of acids and other corrosive materials above waist level.

3. While handling cyanides and other poisons, keep antidote nearby. Poison materials/chemicals should be locked & key should be under authority of QC head.

4. Do not leave apparatus containing corrosive materials at the sink to be washed; always drain out the apparatus before leaving for washing.

5. Bottles containing strong acids should be supported on acid resistant trays. Acid splashes should be washed with water, and then neutralized with sodium bicarbonate solution.

Glassware:

1. Examine glassware for defects before any experiment. Do not use cracked, chipped or otherwise damaged glassware.

2. Reagent bottles and other glassware should be labeled correctly and clearly.

3. Pour liquids in a direction away from label to avoid damaging the label. If any liquid spills on outside of bottles, wash/ wipe the outside of bottle with water before returning to shelf.

4. To remove tight stoppers, top alternatively on each side of stopper. If this does not work and the contents of the bottle are not flammable or toxic, gently warm the neck of the bottle.

5. When a glass tube or rod is it be cut, use gloves and eye protection.

Fire Hazards:

1. Gas cylinders should not be stored in the direct sun and kept at a reasonable distance from any source of heat. Cylinders should be fastened so that they cannot roll or fall. They should be preferably enclosed in a cage.

a) All laboratory staff must be familiar with the position and operation of all fire fighting equipment in their vicinity; these should also be a ‘First Aid’ trained officer in the laboratory.

Electrical Hazards:

Ensure that there are no open connections and bare wires in the department.

Environmental Safety:

1. Waste inflammable solvents which are not miscible with should be poured into bottles intended for this purpose and not into the sink.

2. Dilute solutions of poisons like cyanide, etc., before imputing into the sink and this should be followed by sufficient flushing with tap water. Concentrated solutions should be treated to render them innocuous before pouring down the drain.

3. Reactive chemicals like sodium metal, phosphorous pentoxide, etc. should be converted to non-reactive compounds before pouring them down the drain or disposal.

Safety Aids:

1. Safety goggles/Face Shield

   These are used to protect eyes where splashing may occur or breaking of glass, eg. while working with apparatus under pressure.

2. Gas Masks

   These should be used for protection against toxic gases and fumes and when an operation cannot be carried out in a fuming hood. They are available in the Production departments.

3. Gloves

   Heavy gloves should be used for handling concentrated acid, alkali and other corrosive materials. Where finger dexterity is essential, surgeon's gloves can be used.

4. Laboratory coats and aprons

   These must be worn at all times for protection of body and clothes. Rubber aprons can be worn while handling corrosive materials.

5. Fuming hood cupboard

   Any work involving fumes and harmful gases should be carried out in a fuming cupboard. Make sure the ventilation is in order before commencing the operations.

6. First aid box

   This is equipped with medicines like antiseptic lotions eye wash solution, paracetamol tablets, bandages, pads, ointments for burns etc. and scissors/blade

Accident Report Procedures:

1. Minor Injuries:

   Appropriate first aid should be given in case of burn. The person should then be taken to a medical center for further treatment.

2. Major Injuries:

   Arrange immediate medical aid. Do not move the person except to a position of less danger. Keep the person warm and quiet to minimize the effect of shock.

3. Poison:

   Arrange for medical aid. In the meantime, render the following treatment.

   a) Give large quantities of water, milk or barely water to drink

   b) Where the poison is non-corrosive, an antidote should be given, but not for corrosive poisons. Burning of mouth and lips evinces a corrosive poison.

4. Electric shock:

   Turn off the current at the main switch of the area concerned, to rescue a person in contact with a live switch. If not possible, use rubber gloves or dries woolen materials to protect your hands.

5. Fire:

   Put off the fire with an extinguisher. Switch off electricity to the area concerned. If clothing catches fire, smother the flames by wrapping the person in a blanket or coat or any such material so that the burning area is completely covered. Report immediately to the General Manager/Unit Head.

   The laboratory should be kept clean and tidy at all times by scheduling routine house-keeping procedures.

Glassware and sampling equipments:

1. Soak the empty, used glassware in the basins/tub containing a solution of a detergent in water.
2. Brush each item thoroughly, taking care to remove any stains or grease.
3. Rinse thoroughly with tap water several times and then with distilled water.
4. Dry in an oven or overnight in air and store in the designated place.
5. For microbiological analysis, pipettes and glassware have to be sterilized by heating for 2 hours at 160 C or autoclave at 15 Lbs pressure for 20 minutes.

Pipettes:

1. Soak pipettes after use in a tall jar containing detergent solution for several hours.
2. Drain and rinse with tap water and finally with distilled water and dry.

Burettes:

1. Wash the burettle and stop cock separately.
2. Keep the empty cleaned burettes in inverted position

New glassware:

1. After routine cleaning, treat with a 5 percent solution of sodium carbonate followed by soaking in 1 percent Hydrochloric acid solution.
2. Wash with excess quantity of tap water and then rinse with distilled water. Cylinders, optical cells and curettes should be washed by the analysts themselves.
3. The analysts should wash cylinders, optical cells and curettes themselves.
4. If corrosive chemicals have been used, the analyst should empty the flask himself and rinse it before keeping for washing in the tub.

A volumetric (standard) solution is one of an accurately known strength. Solutions of substances which are not approximate to the one desired and then standardized against a known pure standard. (Primary standard)

1. Prepare the volumetric solution according to the individual procedures as given in General Analytical methods.
2. Store these in bottles with labels indicating the name of the solution, its strength, date of preparing and the person who has prepared it.
3. Standardize these solutions after preparation on the predetermined schedule whenever required; in duplicate. Record the value as an average of 2 observations, which are much closed values.
4. Record the calculations, weights and normalities in the standardization log book.
5. Before use check visually that the contents of the bottle are clear.
6. Volumetric solutions should not differ from the prescribed strength by more than the 10 percent. Where the strength falls below 10 per cent the solution should be replaced.

1. Every sample analyzed in the laboratory has a unique analytical Reference number.

   (A. R. No.) i.e. AOF/ATN/001

   a) The last three digits in the Finished product represent the serial no. of the batch.

   b) The I st 3 alphabets represent the status of the material.

   i.e. AOF - Finished Product

   AOI - Ariane Orgachem Intermediate

   AOR - Raw Material

c) The next three alphabets in the Finished Product A. R. No. represent the short forms of the product.

i.e. ATN - Atenolol

FRU - Frusemide

CPM- Chlorpheniramine Maleate

INT - Intremediate product sent to outside parties.

d) The next alphabet of the AOR in the Intermediate A. R. No. represent the initial of the intermediates. i.e.

L - Lasamide

E - Epoxide

And the last seven digits represent the year and serial No. of batch i.e. 2000 /028.

e) The next digits of the AOR in the Raw material represent the year and the serial No. of receiving of the raw material. i.e. AOR / 2000 / 018

2. Analytical Reference Numbers are assigned in registers maintained separately for samples of raw material, intermediates, packaging materials, finished products and R & D samples. Following details are recorded:

i) Sr. No.

ii) Date of receipt of sampling Advice document

iii) Batch Number.

iv) GR No. (Goods Received Number) (Wherever Applicable) or Sample Reference No. sent to other units on T.I. sheets.

v) Analytical Reference Number (A.R. No.)

vi) Recd from ..... dept/unit/source

vii) Sampled by /Analysed by

viii) Status (Passed, Rejection or Reported) with date

Reference Substances or Reference Standards are authentic samples of highly purified chemicals supplied by the official Pharmacopoeial Commissions. These are used as a basis of comparison for determining the purity of the test specimen.

As these are available only in small quantities, Working Standards are prepared to act as substitutes. These are prepared from in-house manufacture material and standardized against authentic Reference Substances.

Reference Substances:

1. After receiving the Reference Substance, enter the details of the substance in the register meant for the purpose.
2. Store it in an air-conditioned room/refrigerator and use as directed on the label.
3. Whenever official standards get changed by Pharmacopoeial Commissions, replace the old Reference Substances with the current Reference Standards.
4. Each Reference Substances should have a Reference Number with suffix RS.

Working Standards:

1. Choose and standardize the purest possible material matching with the Reference Substance in purity and in other standards. Working Standard should have minimum purity of 99.5 % in anhydrous basis and least possible related impurities
2. After standardization against the Reference Substance, enter the details like date of standardization, purity standards, directions for use and date till which it is valid in the register and working standard protocol and also the label.
3. Store in an air-conditioned room/refrigerator after labeling appropriately.
4. Re-standardize it at about once a year against the official Reference Substance

Persons responsible:

Sampling should be carried out only by trained Q.C. Personnel and should be done in accordance with instructions as per sampling and handling sheet of individual specifications.

Examination of consignment before sampling:

1. Prior to sampling, check the consignment for its identity, quantity and manufacturer's batch number and proper storage as per specifications.
2. See that the containers are not damaged or externally spoiled or contaminated in a way that could result in the contamination of contents.
3. Check that the containers are properly labeled and tagged with consignment details cards.

Method of sampling:

1. Check the details on the GR Notes to be complete.
2. Before opening the container, check that the outsides are free from dust or any material that could contaminate the contents.
3. Affix the Under Test labels on the containers.

4. Choose containers at random (Damaged containers must be sample individually)
5. Mix thoroughly any material liable to inhomogeniety
6. Withdraw the sample from different layers in the material to make the sample as Representative as possible using the appropriate sampling equipment.
7. Keep the samples from individuals
8. Indicate on the sample label the container number from which the sample has been drawn.
9. Identify by means of 'Sampled Pack' sticker labels the containers from which samples have been drawn
10. Ensure proper closer of the containers after sampling.
11. Take the samples to the Quality Control and store in the designated place.

EQUIPMENTS TO BE USED FOR SAMPLING

Sampling equipments and containers should be kept in the custody of the Quality Control Department. These must be cleaned and dried prior to use. For sampling of materials for microbial examination, they must be sterilized before use.

1. Sampling of powder:

   Stainless steel sampling scoop (3 feet in length) to be used and the samples to be stored in virgin food grade self sealing poly bags. 2 x — gms (for two analysis) to be separately kept.

2. Sampling of liquids:

   Glass sampling tube (3 - 4 ft. in length) to be used for the liquid in 200 litters drums and 25/50 ml pipettes to be used for the liquid in 2.5/3.5 litters bottles or tins. The samples to be collected in cleaned and dried bottles with HDPE caps.

SAMPLING LEVEL

1. RAW MATERIALS
   a. If containers are less than 3 in number, sample from every container minimum 20 ml for liquids and 10 g for solids or a specified in the individual specifications of the material.
   b. For consignments having 4 to 100 containers, use the formula $\sqrt{n} + 1$ to determine the number of containers to be sampled (where n = total no. of units in the consignment).
   c. For consignments of over 100 containers sample 1 container from every additional 100 containers.

      For example:

No. of containers	No of samples.
1 - 3	3
4 - 100	\/ n + 1
101 - 200	12
210 - 300	13

Please ensure that when the number of containers are more than 100 - say 200; 12 randomly chosen containers are sampled and no 11 randomly chosen containers from first 100 and 1 from the second 100.

2. BULK DRUGS

Sample every container in the batch.

3. PACKING MATERIAL

Draw the number of samples mentioned in the individual packing material specifications. In case of visual inspection larger population of sample is taken for evaluation of defects as given in specification.

4. QUALITY CONTROL CHECK - LIST FOR SAMPLING

Follow the check - list for sampling of any item.

a. Quality Control check - list for sampling of raw material.

b. Quality Control check -list for sampling of packing materials.

c. Quality Control check - list for sampling of Bulk Finished Products.

d. Quality Control check - list for sampling of Packed Finished Products.

The following is the manner in which various departments send an intimation to Q.C. when any analysis is required.

a) When a consignment of raw materials is received by Stores, intimation is sent to Quality Control Department on a Goods Received (G.R.) Note

b) Whenever manufacture of any bulk drug or formulation is complete, 'Test Request' (T.R.) Forms are sent by Production Departments to the Quality Control Department as an intimation for sampling.

c) The Production Department for all intermediates and in-process samples sends technical Information T.I. sheets Samples are sent by the Production Department alongwith the T.I. sheets.

1. After receiving the G.R. notes/T.R. forms/T.I. sheets, make entries in the relevant Analytical Reference Number register, assigning an A.R. Number to each batch.

2. Collect samples of the material/product form the Production Department/Stores, and keep these in the designated placed. Affix Under

Test labels on the containers. Refer to the sampling checklist for individual items.

3. Check the individual samples for their physical uniformity, eg. Color, nature, appearance, etc.
4. Refer to the General Analytical methods.
5. If they pass preliminary examination, pool these together to form a composite sample.
6. Withdraw a quantity from the composite sample to keep as 'Reserve Sample', equivalent to 2 analyses.
7. Carry out the analysis on the 3rd portion of composite sample.
8. Record all details of tests carried out (like weights, volumes, dimensions, normality, absorbance and other readings) on the reverse side of the Analytical Report/Q.C. copy of the T.I. sheet.
9. Record the results/conclusions on the front of the same sheet or generated on a computer. Attach all spectra and other, printed data pertaining to the tests to the Analytical Test Report.
10. Have all calculations checked by a second chemist.
11. Indicate on the Analytical Test Report and GR note copy whether the same complies with its specification or not by stamping the words 'Passed' or 'Rejected' except in case of samples accompanying T.I. sheets where only results are to be reported. Give reasons in case of rejections.
12. Enter the status of the material in the relevant Analytical Reference Number Register (Passed, Rejected or Reported).
13. Prepare the 'Passed' or 'Rejected' labels and get these affixed under your supervision, in such a manner that the yellow portion of the 'Under Test' label is completely covered. Passed/ Rejected labels should be put on every container.
14. Retain the Analytical Report and one copy of the G.R. Notes and send the remaining copies to the Stores.
15. When a material has to be retested for any reason, 'Quarantine' labels are affixed by the Stores/Production over the 'Passed' labels and T.I. sheet is sent to the Q.C. by the concerned department.
16. Re-analyse the material as above and insure fresh 'Passed' 'Rejected labels.

Sometimes a material is tested at another Unit or an outside laboratory due to non-availability of equipment, facility or for confirmation of results.

The following procedure is followed by the laboratory requesting technical information:

1. Sample the material and abstract a part of the sample sufficient for about 2 analyses.

2. Pack this quantity in polythene bags and label appropriately
3. Send this with a set of two copies of the Technical Information Sheet indicating the tests to be performed, quantity of sample, batch number and sample reference number (A.R. number assigned in your laboratory will be the sample reference number).

   In the case of an outside laboratory send a covering letter.

The following procedure is followed by the testing laboratory (in case of inter laboratory testing):

1. Record the receipt of the sample in the Analytical Reference Number register and assign an A.R. No. to it.
2. Perform the requisite test, recording all calculations and observations on the reverse of both copies of the T.I. sheet and results/concussions on the front.
3. Send the yellow copy of the T.I. sheet, along with a photocopy of the instrument recordings. (Eg. Spectra and other graphs/scans)
4. Retain the white copy of the T.I. sheet with instrument recordings.

Note: The laboratory requesting information should file the results of analyses of the product from both laboratories in the docket (Attach the T.I. sheet and instrument recordings to your Analytical Report)

Reserve samples are preserved for the purpose of re-analysis, Re-analysis may be necessary for tracing back in case of complaints received. The procedure for the handling of reserve samples is given below.

I. Raw Materials/Bulk Drugs:

1. Retain reserve samples of every batch of all raw materials, which are active ingredients in formulations, and all bulk drugs. Certain non-active raw materials may also be kept as reserve samples if indicated in their specifications.
2. When the composite sample is prepared in the laboratory for analysis, abstract a quantity sufficient for at least 2 analyses as the reserve sample.
3. Store these as far as possible in containers simulating the ones in which the material is normally stored or marketed.
4. Affix a label on it.
5. Where the material has been re-tested, retain a sample of the retested material.
6. Make entries in the Reserve Sample Register meant for the purpose.
7. Store these in an air-conditioned room (to maintain their integrity as far as possible so that any re-analysis performed reflects the original analysis)

8. Examine the reserve samples of few batches of active ingredients visually at least once a year unless the examination would affect the integrity of the sample and record the results of the examination.

9. Arrange for the destruction of reserve samples which are not required at regular intervals.

Item	Period of Keeping
Intermediates	Till the finished product batch is released by Q.A.
Key raw materials used in bulk drugs and bulk drugs intermediates.	Till the batch of Bulk Drug is released.

Note: Do not keep reserve samples of corrosive/hazardous chemicals or volatile liquids.

Procedure for the destruction of time expired samples.

1) Identify the batches of products to be destroy by reviewing the Register periodically
2) In the case of items coming under Central Excise, send a list of these in the prescribed format for computation of duty and get their approval.
3) Destroy the samples according to the disposal procedure laid down for the material/product

The procedure given below outlines the method to be followed to establish the stability of products and hence determine their shelf life.

Tentative storage conditions and expire dates are fixed based on stability of new products. These are normally accelerated studies.

The storage conditions and expire dates are monitored and suitably revised if necessary by conducting studies carried out on the product in the pack in which it is marketed under conditions close to market conditions.

Conduction of stability studies is the responsibility of the Quality Assurance Manager/ Q.C. Head/ Manager QA will prepare a stability testing protocol.

Stability studies are carried out on the following batches:

1) Initial R & D or pilot batches (three) at accelerated temperature and humidity
2) Initial production batches (three) at ambient temperature.
3) Regular production batches (one batch a year) at ambient temperature.
4) Batches in which processes and packing material which come in contact with the product have been changed by accelerated temperature and humidity.

Batches to be examined: (Schedule for stability study)

The batches on which the stability studies are to be carried out should be identified in the annual scheduled program of the laboratory.

Quantity of sample:

From the above identified batches withdraw a quantity sufficient for about 10 - 12 analyses. Pack quantities sufficient for each analysis separately in polythene bags and seal the bags. These are enclosed in miniature fiber board drums.

Storage:

Store at room temperature for bulk drugs in case of marketed products at temperature specified for that product or as close to market conditions as follows. Keep samples for accelerated studies under the specified conditions of temperature and humidity as given in the protocol.

Frequency of examination:

Examine the batch at intervals of 3, 6, 9, 12, 18, 36, 48, and 60 months for ambient temperature and at intervals of 1,2,3,4 months at 37 ºC,–45ºC and 65 % ($\pm$ 5 %) humidity.

Tests to be performed:

Perform the tests pertaining to characteristics likely to change on storage and specially those which help in detecting and quantifying degradation products or related impurities. The following tests should be included:

a) Appearance - characteristics

b) L.O.D. / K.F.

c) pH

d) Related substances by TLC or HPLC or GLC. HPLC is the preferred method if applicable

e) IR pattern

f) UV Scan

g) Assay

h) Color Index

Stability testing Protocol:

Draw a protocol for each product on the Stability Testing Form.

New Products - from R & D

Existing product - Production Department

Recording of result:

Record all observations and calculations on Stability Test Report and the results on the Stability Studies Forms.

New Products - from R & D

Existing product - Production Department

Enter results of subsequent analyses of the same batches on the same form. File the S.T. Reporting and the Stability Study Form for each batch at one place.

Present the stability data in graphical form

Assessment of results:

The Quality Assurance Manager and R & D Manager make recommendation of the shelf life of the product depending on these studies.

Documentation is a prime necessity in Quality Assurance. It serves to define systems of control, to reduce the risks of error inherent in oral communication and to ensure that personnel are instructed in the details of and follow procedures. It also helps in tracing the history of each batch of product from the stage of receipt of materials to the release of the batch to the market.

In the analytical laboratory the important aspects of **Quality Control documentation** are:

a) The drawing up of reference documents, which outline procedures, to be followed in assuring the quality of materials, intermediates and finished products.

b) The recording and reporting of results of tests carried out in the laboratory and on the shop floors, and

c) The storage of all documents pertaining to Quality Control

General

1. See that all documents bear a date and number and indicate which documents they supersede.
2. Keep documents up-to-date. Get authorization in advance for any amendment, which is to be made.
3. Where the amendment is permanent, replace the amended document by a newly prepared one at the earliest.
4. Remove the superseded document from active use, retaining a copy for reference.

Specifications:

The Quality Control Head in consultation with the R & D Manager of the Company will write for each material a specification which is relevant to its intended use.

1. Draw up the specification consisting of three parts as given below:

   (Specimens of raw material specification, packaging material specification and finished product specification)

(1) The first part of “Specifications” provides information on sampling and handling of the material. It includes the following:

a) Name of the material with common synonyms. The name given in the Computer Code Manual should be used.

b) Date of the document and the one it supersedes

c) The computer code number for the material.

d) Reference to the pharmacopoeial monograph, where appropriate.

e) Standard packing indicating the pack and pack quantity.

f) Storage requirements

g) Sampling level giving the number of containers to be sampled and the quantity from each container.

h) Quantity of composite samples for analysis

i) Quantity of reserve sample.

j) The period after which the material should not be used in production without retesting indicated by the words ‘Retest after’

k) Hazards and precautions (only for raw materials and bulk drugs)

l) Signature of the person preparing the specification.

m) Signature of the person checking/approving the document

n) Signature of the person authorizing the specification.

(2) The second part of ‘Specifications” provide information on standards and limits. It includes the following:

a) Name of the material.

b) Molecular formula of the material where appropriate.

c) Molecular weight where appropriate.

d) Description of the physical characteristics of the material

e) Solubility

f) Identification

g) List of detailed specifications in quantitative terms, wherever possible.

(3) The third part of "Specifications" provides the experimental details of all the test methods to be used to assess the identity and quality and of the assay of the material. It includes the following:

a) Methods used for all tests to be performed.

b) Where common methods are used, do not give details, but gives a reference to the General Analytical Methods (GAMS).

2. While writing the specifications and methods of analysis:

a) List the tests in the same order as they are listed in the relevant pharmacopoeia.

b) Indicate the specifications, which are additional to the pharmacopoeia ones by means of an asterisk (*)

c) Mark by means of a double asterisk (**) those tests are not performed on a routine basis and indicate when these are performed.

3. Review specifications on a yearly basis.

RECORDS

1. Note key observations, readings, and calculations, directly on the reverse side of the Analytical Reports.

2. Enter the name of the material under test, batch number, and date of analysis before carrying out the analysis.

3. Where analysis of the sample is spread over a number of days, record the date on which each test was carried out.

4. Record the results on the front side of the Analytical Report.

5. Enter the date of testing, A.R. Number, batch number and test details on all spectra and other instrument records and attach these to the main report.

6. Calculate the results of assay to one decimal place more than that indicated in the specification but round up and report only to same number of places given in the specification.

7. Generate the report with the help of computer whenever possible

8. Get all calculations checked by a second chemist.

EQUIPMENT OPERATING PROCEDURES

Operating procedures are available for every instrument in each laboratory. These are kept in the form of readily referable documents.

Keep these at a place for ready reference and operate the instrument only when you have ready and understood the procedure. Specimen of a typical operating procedure

CALIBRATION AND MAINTENANCE OF INSTRUMENTS

Procedures for maintenance and calibration of equipment and schedules for the same are drawn up in the laboratory.

Calibrate the instruments according to the procedure and schedule periodically and enter the results in a record log kept for each instrument

The laboratory should be kept clean and tidy at all times by scheduling routine house-keeping procedures.

The Q.C. head at every unit prepares and submits a monthly report to the General Manager. A copy of this is also sent to the Q.A. Manager at the Corporate Office

In general it contains information under the following headings:

A. Statistics of Analytical work:

(No. of samples received, the number pending, rejections, etc,)

B. Reject Analysis:

(Follow-up on rejects in consultation with Production and Purchase to review effect on Production Planning.)

C. Problems:

(Encountered or anticipated, and their solutions or proposed solutions).

D. Personnel:

(Their significant contributions, training imparted to them etc.)

E. Improvements:

(Made or proposed)

F. Product Quality:

(Stability reviews, complaints, review of specifications, etc.)

VALIDATION OF ANALYTICAL METHODS

The word validate means to confirm. In other words, validation involves confirming whether the procedure, system or method actually achieves what it is supposed to.

There are two major components of validation:

a) The procedure or method must give accurate results, and

b) It must give reproducible results.

Validation normally involves the comparison of the method to be validated with a known and accurate method or by comparing the results obtained with the method in question with the results obtained on a known sample. Known samples are usually reference standards of high purity supplied by pharmacopoeial commission.

Analytical methods given in the pharmacopoeia, in general, need not be validated because they are certified to be accurate and have been tested to give reproducible result. However, if the method is not official in the pharmacopoeia, then it must be validated.

The following is the suggested methodology for carrying out validation on analytical methods.

1. Designate a team which will do the validation. In general, it is desirable to have on this team at least one member who is not involved in routine analysis (say, a member assigned for R & D /Instrumental analysis).
2. Write a protocol which gives:
   a) The name of the method to be validated.
   b) The purpose of the experiment.
   c) The method to be used giving details of all steps to be followed

Example:

i) Test a known standard for its purity by the method to be validated. See whether the results are comparable with its known assay.

ii) Test a sample for its purity by the method to be validated as also by a known pharmacopial method. See whether the results are comparable.

3. In order to remove variation due to 'chance', it is recommended that the procedure be repeated in duplicate.
4. The method is accurate if the results obtained with the method being validated do not differ from the known results by more than +/- 2 percent.
5. It is reproducible if the results obtained in the replicate analysis using the method being validated do not differ by more than +/- 2 percent.
6. Before carrying out the Validation studies, ensure that all glassware, instruments, etc., are calibrated to ensure.

HANDLING OF COMPLAINTS

A product complaint may be considered as formal expression of dissatisfaction with any of the Company's products. It serves as the primary means of obtaining feed back about product quality.

A) Bulk Drugs and Intermediates

Intra-Unit Complaints

Complaints from one unit's of the company to another are normally received by the Head of the Manufacturing Unit. Depending upon the nature of the complaint, a sample of the material is also sent along with the complaint.

The Q.A. of the manufacturing unit initiates the investigation of the complaint with the head of the Q.C. where a complaint sample has been sent, the Q.C. examines it along with its reserve sample.

In other cases, a reference is made to the original analytical report and the reserve sample is reanalysed by the Unit Q.C. and a report of the findings on a Technical Information sheet (TI Sheet) is sent to Q.A.

Q.A. discusses the report with the General Manager of the Unit. The likely reason for the complaint is investigated by the General Manager. Depending

upon the results of the investigation, the General Manager communicates to the Unit Head of the Company whether the material is to be recalled or could be used after suitable reprocessing at the complaining unit. In the later case, corrective action is suggested in consultation with R & D.

When reprocessing is done at the complaining unit, the reprocessed material is analyzed and cleared by the QC of that unit. A copy of the analytical report is sent to the Q.C. of the original manufacturing unit.

HANDLING OF PRODUCT COMPLAINTS

I & II Complaints on physical and packaging defects

1) The Marketing department records the details of the complaint, using a set for each complaint.
2) The Marketing department also acknowledges receipt of the complaint to the complainant
3) The Executive sends the sample and the set of Product Surveillance forms to the Head of the Unit, which had manufactured the product.
4) The Head of the Unit refers the complaint to the QA. QA in consultation with the QC Lab and the concerned manufacturing department, investigates the complaint and reports the findings to the Unit Head
5) The Unit Head communicates his findings to the Executive at Bombay Central.
6) On receipt of the Report, the Exec.