Guidance Document

for
Drafting and Formatting of Monographs for Indian Pharmacopoeia

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Guidance Document

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INDIAN PHARMACOPOEIA

1.1 Introduction

The Indian Pharmacopoeia (IP) is a compilation of official standards for drugs manufactured and/or marketed in India. The full name or title of the book is Indian Pharmacopoeia abbreviated I.P. or IP, Addendum to the pharmacopoeia is title as Addendum to IP.

Standards in the IP are expressed in the form of specifications and test methods for determining compliance with such standards. Specifications that are applicable to any pharmaceutical article are compiled in a monograph.

A monograph states the quality or test parameters, the acceptance criteria and details of the tests that are to be performed to determine compliance with the criteria. In other words, a pharmacopoeial monograph provides a reliable basis for making an independent and objective judgement as to the quality of a pharmaceutical substance.

As IP standards are statutory, it is important that the contents of monographs are unambiguous, acceptance criteria are clearly spelt out and the methods of evaluation provide all the details for carrying out the tests and assays, including the equipment, reagents and other ancillary materials that are to be used. To ensure that this requirement is uniformly and consistently met, guidance is provided in the following pages on the manner of drawing up of monographs and test methods and other relevant information. The exact manner of describing the tests, standards and reference to the general testing method numbers are also given.

It shall be ensured that statements made in the monographs do not conflict with those stated in the General Notices, General Texts and with any information given in other sections of the Pharmacopoeia.

1.2 Purpose of guideline

This document is a guide for drafting and elaboration of the monographs to the stakeholders of the Indian Pharmacopoeia especially industries, testing laboratories and academicians. The format mentioned in the guideline is to be applied while drafting of new monograph for its inclusion in IP. The aim is to provide guidance for drafting clear unambiguous texts, with similar requirements presented in same the way in each monograph. The guideline is illustrated by examples, for useful indication of the text.

1.3 Contents of the Pharmacopoeia

The technical part of the pharmacopoeia shall be broadly divided into the following sections:

1. Introduction
2. General Chapters
3. General Monographs
4. Test methods
5. Reference Data
6. Reagents and Solutions
7. General Tests
8. Index

1.3.1 Introduction

The Scientific Director of the Indian Pharmacopoeia Commission (IPC) shall approve this part after all the contents of the pharmacopoeia have been finalised. It shall briefly give the background to the edition and describe the salient features including the admissions and omissions from the previous edition.

1.3.2 General Notices

The purpose of the General Notices is to provide the basic guidelines to the interpretation and application of the standards, tests, assays and other specifications of the pharmacopoeia, as well as to the statements made in the monographs, test methods and appendices. Included, among other things, is the system of nomenclature of chemical compounds that is to be adopted. Recommendations on storage of drugs and specific labelling requirements may also be given.

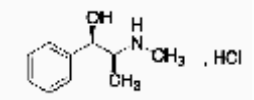
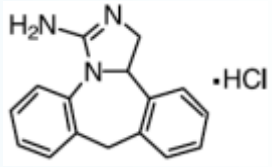
1.3.3 Formats and Contents of Monographs

Format	• One Column Format; • Text are written in Present Tense; • Operations to be carried out are written in Imperative and result is expressed in Present Indicative; • Numbers are written as Figures eg: 1 ml, 20 g per liter ; • 'per cent' is written in full, not as '%'; • Temperature to be indicated as symbol 'o', Celsius should not be written e.g.- determined by drying in an oven at 105°. • In cases where limits are expressed, the units are repeated: e.g.- + 0.10° to + 0.10° or 75 per cent to 140 per cent

	• Expression of time i.e. hours, minutes and seconds are written in full:e.g.- 1 hour or 20 minutes
Monograph Title	• Times New Roman; 14 pt; Bold • Printed with initial letters in capitals and other letters in small case e.g.- Cytarabine Injection or Ramipril and Hydrochlorothiazide Tablets • Synonyms, if any, shall be printed two spaces below the main title; 11 pt and shall not be in bold letters.e.g- **Cytarabine Injection** β-Cytosine Arabinoside Injection
Monograph Font	• Text matter: Times New Roman; 10 pt • Headings – Identification & Tests : Times New Roman; 11 pt; Bold • Single-line spacing • Alignment Justified • Each test parameter and accompanying text shall be separated from the other by a space of 1.5 lines
Heading of Tests	• Times New Roman; 10 pt; Bold e.g.- pH, Related substances, Assay
Reagents, buffer solutions, chemicals	• Reagents, buffer solutions, chemicals other substances that are described or defined in the Pharmacopoeia shall be in italics. e.g.- *0.1M perchloric acid* • However, where a specific reagent is prepared for a specific test in a monograph and reference to it is made subsequently in the monograph it need not be in italics.
Reference Substances	• Chemical Reference Substances (CRS) or Botanical Reference Substances are indicated in Italics followed by the letters RS e.g.- *pyridoxine hydrochloride RS*
Note:	Italic types shall also be used for the systematic names of plants and micro-organisms, and for some sub-headings of tests and texts (such as precautions to be observed while performing the tests, or which identification tests may be omitted etc) and for some parts of the chemical names.

Monograph Development on Active Pharmaceutical Ingredients (API) (Bulk Drug Substances)

MONOGRAPH DEVELOPMENT ON ACTIVE PHARMACEUTICAL INGREDIENTS (APIs) BULK DRUG SUBSTANCES

S. No.	Content	Monograpzzh	Example
1.	Title of the Monograph	Name of the item printed in bold letters in Times New Roman font size 14 pt (Times New Roman). The International Non-proprietary Name (INN) approved by the World Health Organization (WHO) shall be used Subsidiary or abbreviated title or synonym (if any) may be shown two spaces below the main title (in ordinary letters); 11 pt The main monograph headings viz. Identification and Tests etc. shall be in Times New Roman size 11 pt, and the headings of the individual tests in size 10 pt, and all in bold letters.	**Sodium Aminosalicylate** Sodium PAS **Cetirizine Hydrochloride** Cetirizine Dihydrochloride **Ephedrine Tablets** Ephedrine Hydrochloride Tablets
2.	Formula	1. Structural (Graphic) Formula 2. The molecular formula on the left and the molecular weight expressed to one decimal place on the right, two spaces below the graphic formula	Ephedrine Hydrochloride  $C_{10}H_{15}NO,HCl$ Mol. Wt. 201.7 Epinastine Hydrochloride  $C_{16}H_{15}N_3,HCl$ Mol. Wt. 285.8

3.	**Chemical Name**	A statement of the chemical name, two spaces below the molecular formula, where the substance is a distinctly definable chemical entity, as follows: XXX is YYY, where XXX is the name of the item as given in the title of the monograph, and YYY is the chemical name sanctioned and employed by the International Union of Pure and Applied Chemistry (IUPAC). *Note- Guidance on steriochemical configuration, the sign of the optical rotation of enantiomers etc shall referred from the General Notices of the Pharmacopoeia.*	Sodium Aminosalicylate is sodium 4-amino-2-hydroxy-benzoate hydrate. Ethionamide is 2-ethylpyridine-4-carbothioamide. Carbamazepine is *5H-dibenz(b,f)* azepine-5 carboxamide
4.	**Statement of Purity**	A definitive statement of the purity of the article, two spaces below Chemical name, and expressed in the following manner: AB contains not less than X per cent and not more than Y per cent of the chemical entity expressed as the molecular formula, calculated on the dried basis (where a test for loss on drying is specified), or on the anhydrous basis (where a test for water is specified) Where, AB is the pharmacopoeial name of the article, X and Y are the lower and higher percentage figures, respectively, expressed to one decimal place only.	Sodium Aminosalicylate contains not less than 99.0 per cent and more than 101.0 per cent of $C_7H_6NNaO_3$, calculated on the anhydrous basis. Ethionamide contains not less than 98.5 per cent and not more than 101.0 per cent of $C_8H_{10}N_2S$, calculated on the dried basis. Cyclophosphamide contains not less than 98.0 per cent and not more than 102.0 per cent of $C_7H_{15}Cl_2N_2O_2P$, calculated on the anhydrous basis. Erythromycin has potency not less than 920 Units per mg, calculated on the anhydrous basis.

			Bacitracin Zinc has a potency of not less than 60 Units of bacitracin activity per mg, calculated on the dried basis.
5.	Category	Category is to be given as informative part of the drug. Only the category needs to be mentioned	**Sodium Aminosalicylate** **Category.** Antitubercular **Epinastine Hydrochloride** **Category.** Antihistaminic
6.	Dose	Dose is to be given in g or mg per day.	**Sodium Aminosalicylate** **Dose.** 10 to 15 g daily, in divided doses **Epinastine Hydrochloride** **Dose.** 5mg to 50 mg daily.
7.	Description	A brief description of the physical form of the material, including colour, texture, whether hygroscopic, odour, if readily apparent, and any other characteristic. ***Note-*** The indefinite article 'A' shall be used before the description	**Description.** A white to cream coloured crystalline powder. **Description.**A white, crystalline powder or colourless, transparent crystals, efflorescent. **Description.** A pale yellow oil with slight, but not rancid odour **Description.** A colourless and odourless gas.
8.	***Note:*** The following sections deal with the tests to be performed. Where reference is made to a general test procedure, the relevant number of the procedure is mentioned in brackets immediately after the test heading. However, in the following cases, the brackets may appear where the reference to the appendix is needed or at the end of the statement. 1.3.3 thin-layer chromatography (2.4.17) Infrared absorption spectrophotometry (2.4.6) etc., In the former case, a dot should be put after the bracket and in the latter, a dot or comma depending on whether the text ends or continues, respectively. There should not be a comma before the brackets.		

9.	**Identification**	At least two or three identification tests, starting with physical and instrumental tests and ending with general chemical reactions shall be given. The tests shall be marked with the letters A, B, C and so on followed by a dot and then the text after one space. The texts will naturally vary from test to test but given below is the mode of expression of certain common tests: If more than one specific test are given as infrared absorption spectrophotometry and other tests A, B, C, D and E. One line should be written in italics as *"Test A may be omitted if tests B,C,D and E are carried out and Tests B,C,D and E may be omitted if test A is carried out".* Infrared absorption spectrophotometry- This shall normally be the first identification test, where applicable. Determine by infrared absorption spectrophotometry (2.4.6) (test method number to be put within the brackets). Where necessary, the specific manner of preparing the sample may be given. Compare the spectrum with that obtained with yyyRS (where yyyRS is the Reference Substance) or with the reference spectrum of yyy. Note- The acceptance criterion need not be repeated in the monographs. It shall be given in the test method itself.	**By Infrared Absorption spectrophotometry** Identification A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *ceftazidime RS* or with the refrence Spectrum of ciftazidime. **By UV spectrophotometry** Identification B. Dissolve 20.0 mg of the substance under examination in water and dilute to 100.0 ml with the same solvent. Dilute 10.0 ml of this solution to 100.0 ml with *water*. The specific absorbance (2.4.7) determined at 235 nm is 360 to 390. OR **Identification B.** When examined in the range 230 nm to 360 nm (2.4.7), a 1.0 per cent w/v solution of xxxx shows an absorption maximum at about ….nm. **By Thin layer chromatography** **Identification C.** Determine by thin-layer chromatography (2.4.17), coating the plate with xxxxx. *Mobile phase.* A mixture of 50 volumes of *ethanol (95 per cent),* 30 volumes of *water,* 10 volumes

of strong *ammonia solution* and 10 volumes of *ethyl acetate.*
Test solution. Dilute a suitable volume of the substance under examination to obtain a solution containing 2 per cent w/v of Calcium Gluconate.

Reference solution. A 2 per cent w/v solution of *calcium gluconate* RS in *water*, heating if necessary, to 60° in a water-bath to effect solution.

Apply to the plate 5 µl of each solution. After development, dry the plate at 100° for 20 minutes, cool and spray with a 5 per cent w/v solution of *potassium dichromate* in a 40 per cent w/w solution of *sulphuric acid*. After 5 minutes the principal spot in the chromatogram obtained with the test solution corresponds to that in the chromatogram obtained with the reference solution.

If the plate spray with the reagent it should be dried by heating and examine. The principal spot in the chromatogram obtained with the test solution corresponds to that in the chromatogram obtained with the reference solution.

By HPLC

HPLC test- Usually when this procedure is used for the identification test the assay is also done by the same procedure. In such cases, the identification test shall state the agreement between the principal peaks in the chromatograms of the test and reference solutions.

Identification D. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Where the HPLC test is used only for the identification test and not for the assay the manner of describing the test shall be similar to that given below in the examples for Related substances or Assay where such a test is to be employed, but the acceptance criterion will be as given in the example above except that the words "In the Assay" shall be omitted.

By Chemical Tests

Chemical reactions- Texts depend on the nature of the tests.

Dissolve about 10 mg in 1 ml of *sulphuric acid*. An intense yellow colour develops.

OR

Dissolve about 10 mg in 2 ml of *dilute hydrochloric acid* and heat on a water-bath for three minutes. Add 3 ml of *sodium carbonate solution* and 1 ml of 2 per cent w/v solution of *sodium*

nitroprusside. A violet-red colour develops. *General chemical reactions-* **Identification. E.** It gives reaction (a) of sodium (2.3.1) OR **Identification. E.** The solution prepared for identification test A gives reactions (a) and (b) of potassium (2.3.1).			
10.	Test Appearance of Solution	Method for preparation of the test solution is to be given. The solution is clear (2.4.1) and not more intensely coloured than reference solution xx OR The solution is not more opalescent than opalescence standard (2.4.1)	**Appearance of solution.** Dissolve 4.0 g in 10 ml of *water*. The solution is clear (2.4.1) and not more intensely coloured than reference solution BYS5 (2.4.1) OR The solution is not more opalescent than opalescence standard OS2 (2.4.1).
11.	pH	Method for preparation of solution if applicable is to be given.	**pH** (2.4.24). 4.0 to 6.0, determined in a 0.25 per cent w/v suspension. **OR** **pH** (2.4.24). 3.5 to 4.5.
12.	Melting range	A range is to be provided	**Melting range** (2.4.21). 192° to 195°
13.	Specific optical rotation	+xxx^{0}to +xxx^{0}or -yyy^{0}to -yyy^0. The method of preparing the test solution may be given in some cases. Results to be reported to only one decimal place.	**Specific optical rotation** (2.4.22). +70.0° to +73.0°. Weigh accurately about 0.5 g, dissolve in *water* and dilute to 20.0 ml with the same solvent. OR **Specific optical rotation** (2.4.22). +70.0° to +73.0°, determined in a 1.0 per cent w/v solution in *methanol*.

14.	**Light absorption**	Method of preparing the test solution shall be given. The ratio of the absorbance at about ….nm to that about …..nm is not more than …..	**Light absorption** (2.4.7). When examined in the range 230nm to 360nm, a 0.0015 per cent w/v solution in *methanol* shows an absorption maximum only at about 286 nm. The ratio of the absorbance at about 240 nm to that at about 286 nm is not more than 0.12.
15.	**Light absorbing impurities**	Method of preparation of test solution is to be given. The absorbance (…….) of the resulting solution, determined at ….nm is not more than…… calculated on the…….basis.	**Light-absorbing impurities.** Dissolve 0.10 g in a mixture of 1 volume of *1M hydrochloric acid* and 99 volumes of *methanol* and dilute to 10.0 ml with the same mixture of solvents. The absorbance (2.4.7) of the resulting solution, determined within 1 hour of preparing the solution, at 490 nm is not more than 0.07.
16.	**Related Substances**	Details of the method-usually by thin-layer (2.4.17), or liquid chromatography (2.4.14) or gas chromatography (2.4.13) shall be given.	**For Ethosuximide:** **Related substances.** Determine by gas chromatography (2.4.13). *Test solution (a)* Dissolve 1.0 g of

the substance under examination in sufficient *chloroform* to produce 10.0 ml.

Test solution (b). Dilute 5.0 ml of test solution (a) to 10.0 ml with a 0.01 per cent w/v solution of *anthracene* (internal standard) in *chloroform.*

Reference solution (a). Dissolve 10 mg of *2-ethyl-2-methylsuccinic acid* in sufficient *chloroform* to produce 10.0 ml.

Reference solution (b). Dilute 1.0 ml of test solution (a) to 100.0 ml with *chloroform.* To 1.0 ml of the solution add 5 ml of the internal standard solution and sufficient *chloroform* to produce 10.0 ml.

Reference solution (c). Dilute 1.0 ml of test solution (b) to 50.0 ml with *chloroform.* Add 1 ml of this solution to 1 ml of reference solution (a), add 5 ml of the internal standard solution and sufficient *chloroform* to produce 10 .0 ml.

Chromatographic system – a glass column 2 m x 2 mm, packed with silanised diatomaceous support (125 to 180 mesh) impregnated with 3 per cent w/w polycyanopropylmethyl- phenylmethyl siloxane, – temperature: column.165°, inlet port and detector. 240°, – flow rate: 30 ml per minute, using nitrogen as the carrier gas. Inject 1µl of test solution (a). The test is not valid unless the resolution between the peaks corresponding to 2-ethyl-2-methylsuccinic acid and ethosuximide is not less than 4.			
17.	Arsenic	Method of preparing the test solution shall be given. The resulting solution complies with the limit test for arsenic (2.3.10) (x ppm).	**For Boric Acid** **Arsenic** (2.3.10). Dissolve 1.0 g in 50.0 ml of *water* containing 2 g of *citric acid* and add 0.1 ml of *stannous chloride AsT* and 10 ml of *hydrochloric acid*. The resulting solution complies with the limit test for arsenic (10 ppm).
18.	Heavy metals	……g complies with limit test for heavy metals (…. ppm). Prepare the standard using …. ml of lead standard solution (……ppm) Where the method of preparing the test solution is different from the standard, the method shall be described and the manner of doing the test shall then be given.	**Heavy metals** (2.3.13). 1.0 g complies with the limit test for heavy metals, Method B (20 ppm). OR **Heavy metals** (2.3.13). 2.0 g complies with limit test C for heavy metals (20 ppm). Prepare the standard using 4 ml of *lead standard solution (10 ppm Pb)* OR **Heavy metals** (2.3.13). Dissolve 2.0 g in 4 ml of a 40 g/l solution of *sodium hydroxide* and dilute to 20 ml with *water*. 12 ml of the solution complies with limit test A for heavy metals (2.3.13).

19.	Iron	Method of preparation of the test solution to be given. The solution complies with the limit test for iron (……ppm)	**Iron** (2.3.14). Dissolve 2.0 g in 20.0 ml of *water*. The solution complies with the limit test for iron (20 ppm).
20.	Chlorides	Method of preparation of the test solution to be given. The solution complies with the limit test for chlorides (……ppm).	**Chlorides** (2.3.12). Dissolve 1.0 g in *water*, add 4 ml of *dilute nitric acid* and dilute to 15 ml with *water*. The solution complies with the limit test for chlorides (50 ppm)
21.	Sulphates	Method of preparation of the test solution to be given. The solution complies with the limit test for sulphates (…..ppm).	**Sulphates** (2.3.17). Dissolve 5.0 g in *water* and dilute to 15 ml with *water*. The solution complies with the limit test for sulphates (200 ppm).
22.	Non-volatile substances	Not more than…….per cent. The method of performing the test may be given.	**Non-volatile substances.** Not more than 0.002 per cent.Evaporate 100.0 g to dryness on a water-bath after having verified that it complies with the test for peroxides, and dry in an oven at 100° to 105°. The residue weighs not more than 2 mg.
23.	Residual Solvents	Determine by head-space gas chromatography (2.4.13) using the ABC method. The content of xxxx is not more than …ppm, and the content of yyyy is not more than…..ppm. For ABC the specific method given in the test method section shall be stated, and for xxxx and yyyy, the names of the solvents shall be mentioned. Chromatographic system. The details shall be given	
24.	Microbial Contamination	Limit for microbial count is to be provided and the method used.	**Microbial contamination** (2.2.9). Total microbial count is not more than 10^3 bacteria and 10^2 fungi per gram, determined by plate count. It complies with the tests for *Escherichia coli, Salmonella and Shigella.*

			OR **Microbial contamination** (2.2.9). Total microbial count is not more than 10^3 bacteria and 10^2 fungi per gram, determined by plate count. 1 g is free from
25.	Bacterial endotoxin	**Bacterial endotoxins.** If intended for use in the manufacture of sterile dosage forms without a further procedure for the removal of bacterial endotoxins, not more than XX Endotoxin Units per mg.	**Bacterial endotoxins** (2.2.3). Not more than 0.07 Endotoxin Unit per mg. OR **Bacterial endotoxins** (2.2.3). Not more than 0.2 Endotoxin Unit per mg of cyclophosphamide
26.	Sterility	**Sterility.** If intended for use in the manufacture of sterile dosage forms without a further appropriate sterilisation procedure, it complies with the test for sterility (2.2.11)	**Sterility** (2.2.11). Complies with the test for sterility.
27.	Pyrogens	It complies with the test for pyrogens. The quantity to be injected shall be given.	**Pyrogens** It complies with the test for pyrogens (2.2.8). Inject per kg of the rabbit's weight a volume equivalent to 0.5 g of immunoglobulin but not more than 10 ml per kg of body weight.
28.	Sulphated ash	Limits to be mentioned as- Not more than ….. per cent.	**Sulphated ash** (2.3.18). Not more than 0.1 per cent. OR **Sulphated ash** (2.3.18). 14.0 to 28.0 per cent, determined on 1.0 g, using a mixture of equal volumes of sulphuric acid and water, and calculated on the dried basis.
29.	Water	Not more than …. per cent, determined on …… g	Water (2.3.43). Not more than 2.0 per cent, determined on 0.5 g.

30.	Loss on drying	Not more than.....per cent, determined on XXX g by drying in an oven at xxx° to yyy°.	**Loss on drying** (2.4.19). Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 100° to 105°.
31.	Assay	Although there are many types of assay, they broadly fall into one or the other of the ones given here. Assay can be performed by any of these methods: **By HPLC method** **Assay.** Determine by liquid chromatography (2.4.14). *Test solution*. Directions for preparing to be given *Reference solution.* – do – Chromatographic system: • details of the column, • mobile phase composition and flow rate, • detector and wavelength setting, • injection device (if any), and • any other detail. *Note*- Commas are to be put after each item except the last where a full stop is to be given. Instructions for carrying out the determination, including the volumes to be injected, sequence of injections etc. Calculate the percentage content of xxxx, where xxxx is the chemical entity mentioned in the opening purity statement. OR **Assay.** Determine by gas chromatography (2.4.13).	**By HPLC method** **Assay.** Determine by liquid chromatography (2.4.14). *Test solution.* Weigh accurately a quantity of the substance under examination containing 25 mg of cefuroxime and dissolve in sufficient *water* to produce 25.0 ml. Immediately transfer 5.0 ml of the resulting solution to a 100-ml volumetric flask, add 20.0 ml of a 0.15 per cent w/v solution of *orcinol* (internal standard) in *water*, dilute to volume with *water* and mix. *Reference solution.* Disperse a quantity of *cefuroxime sodium RS* equivalent to 25 mg of cefuroxime in a similar manner. Chromatographic system – a stainless steel column 15 cm x 4.6 mm, packed with hexylsilane bonded to porous silica (5 µm), – mobile phase: a mixture of 100 volumes of *acetate buffer pH 3.4* and 10 volumes of *acetonitrile,* – flow rate: 2 ml per minute, –spectrophotometer set at 254 nm, –injection volume: 10 µl. Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent. Inject the reference solution and the test solution.

		OR **Assay.** Method for preparation of the test solution to be given. Measure the absorbance (2.4.7) at the maximum at …..nm. Calculate the content of ……..taking the specific absorbance to be ….. OR **Assay.** Method for preparing the test solution to be given. Titrate with ……. Determine the end-point potentiometrically (2.4.25) Carry out a blank titration. 1 ml of titrant is equivalent to….. g of…….	Calculate the content of $C_{16}H_{15}N_4NaO_8S$. **By Gas Chromatography** **Assay.** Determine by gas chromatography (2.4.13). *Test solution.* Dissolve 0.1 g of the substance under examination in 10 ml of the *ethanol (95 per cent).* *Reference solution.* A solution containing 0.6 per cent w/v of *cetyl alcohol RS* and 0.4 per cent w/v of *stearyl alcohol RS* in *ethanol (95 per cent).* Dilute 1.0 ml of this solution to 10.0 ml with the same solvent. Chromatographic system

– a capillary column 30 m x 0.32 mm packed with poly(dimethyl)siloxane (1 µm),
– temperature: column 150° -250° from 0-20 minutes and 250° from 20-40 minutes,
– inlet port and detector at 250°,
– flame ionization detector,
– flow rate: 1ml per minute, using nitrogen as the carrier gas.

Inject 1 µl of the reference solution. The test is not valid unless the resolution between the peaks due to cetyl alcohol and stearyl alcohol is not less than 5.0.

Inject the reference solution and the test solution.

Calculate the content of cetyl alcohol, $C_{16}H_{34}O$ and stearyl alcohol, $C_{18}H_{38}O$.

By UV Light Absorption

Assay. Weigh 0.2 g and dissolve in sufficient *water* to produce 200.0 ml. Dilute 5.0 ml to 250.0 ml with *water* and measure the absorbance of the resulting solution at the maximum at about 241 nm (2.4.7). Calculate the content of $C_{22}H_{28}FNa_2O_8P$, taking 297 as the specific absorbance at 241 nm.

By Titrimetry

Assay. Weigh accurately about 0.15 g and dissolve in a mixture of 10 ml of *anhydrous acetic acid* and 40 ml of *glacial acetic acid*. Titrate with *0.1M perchloric acid.* Determine the end-point potentiometrically (2.4.25) Carry out a blank titration.

1 ml of *0.1 M perchloric acid* is equivalent to 0.01827 g of $C_6H_{15}ClN_2O_2$.

32.	Storage	Special storage conditions, if any shall be specified. Note: The type of container need not be given except in very rare cases. e.g. Store in single dose or multiple dose containers.	**Storage.** Store at a temperature not exceeding 30°. If the substance is sterile, store in a sterile, airtight, tamper-proof container. OR **Storage.** Store protected from light and moisture OR **Storage.** Store protected from light, at a temperature not exceeding 30° OR **Storage.** Store protected from light and moisture at a temperature not exceeding 30°
33.	Labelling	Any special labelling statements specific to the product and also not stipulated in the Drugs Rules shall be given.	The label states whether or not the material is intended for the manufacture of sterile preparations.

Monograph Development on Dosage Forms (Formulation)

MONOGRAPH DEVELOPMENT ON DOSAGE FORMS (FORMULATION)

S. No.	Content	Monograpzzh	Example
1.	Title of the Monograph	The following or some of the following information in this column shall be included in the monographs of dosage forms that contain synthetic APIs Name of the item printed in bold letters in font size 14 pt (Times New Roman). Alternate titles/or synonym, if any shall be given one space below the main title in Font size 11 pt (Times New Roman)	**Oxytetracycline Injection** **Trimethoprim and Sulphamethoxazole Oral Suspension** Sulphamethoxazole and Trimethoprim Oral Suspension; Co-trimoxazole Oral Suspension; Co-trimoxazole Mixture **Trimethoprim and Sulphamethoxazole Tablets** Sulphamethoxazole and Trimethoprim Tablets; Co-trimoxazole Tablets
2.	Definition/ Description	A definition of the preparation in terms of the active ingredient(s) together with information on its presentation except where the nature of the product is evident from the title. For parenteral preparations information shall be provided whether it is a solution, a suspension, a dry powder or a concentrate for dilution. Also to be mentioned as information on the nature of any additives (buffers, antimicrobial preservatives etc.)	Betamethasone Injection is a sterile solution of Betamethasone Sodium Phosphate in Water for Injections. Clotrimazole Cream contains Clotrimazole in a suitable base. Chloramphenicol Eye Drops are a sterile solution of Chloramphenicol in Purified Water. Aciclovir Oral Suspension is a suspension of Aciclovir in a

		present; for other sterile preparations the nature of the vehicle shall also be stated For semi-solid preparations information on the type of base (water-in-oil, oil-in-water) etc. shall be given. For tablets information on whether or not the tablets are coated and, if so, the type of coating shall be given. For injections that are supplied as solids that are to be constituted before use.	suitable flavoured vehicle. Ethosuximide Syrup is a solution of Ethosuximide in a suitable flavoured vehicle. Cefotaxime Injection is a sterile solution of Cefotaxime in Water for Injections. It is prepared by dissolving Cefotaxime Sodium for Injection in the requisite amount of Water for Injections before use.
3.	Content statement	XXXX contain not less than……per cent and not more than……per cent of the stated amount of YYY (active ingredient), ZZZZZ (molecular formula).	Alprazolam Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of alprazolam, $C_{17}H_{13}ClN_4$. Phenelzine Sulphate Tablets contain phenelzine sulphate equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of phenelzine $C_8H_{12}N_2$. Salbutamol Inhaler contains not less than 80.0 per cent and not more than120.0 per cent of the amount of salbutamol, $C_{13}H_{21}NO_3$ stated to be delivered by actuation of the valve. Chloramphenicol Eye Drops contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$.

4.	Identification	Method of treating the sample and preparing the test solution shall be given, where required, followed by the details of the test in the manner shown in Section A.	A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *cholecalciferol RS* or with the reference spectrum of cholecalciferol. B. Dissolve 1 mg in 1 ml of *1,2-dichloroethane* and 4 ml of *antimony trichloride* solution; a yellowish-orange colour is produced. C. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.
5.	Dissolution	Dissolution (2.5.2). Apparatus No, medium volume and composition, speed and time of rotation of spindle. The volume of medium to be withdrawn and subsequent operations for treating the aliquot and the manner of calculating the content shall be given.	**For Diethylcarbamazine Tablets** **Dissolution** (2.5.2). Apparatus No. 1, Medium. 900 ml of *water*, Speed and time. 50 rpm and 45 minutes. Withdraw a suitable volume of the medium and filter. Dilute the filtrate, if necessary, with an equal

volume of a 6.248 per cent w/v solution of *potassium dihydrogen phosphate*. Carry out the determination as described in the Assay. Calculate the content of $C_{10}H_{21}N_3O,C_6H_8O_7$ using a solution of known concentration of *diethylcarbamazine citrate RS* in a 3.124 per cent w/v solution of *potassium dihydrogen phosphate*.

D. Not less than 75 per cent of the stated amount of $C_{10}H_{21}N_3O, C_6H_8O_7$.

For Diclofenac Prolonged-release Tablets

Dissolution (2.5.2). Complies with the test stated under Tablets.

A statement should be written in Italics after title of the monograph

Diclofenac Prolonged-release Tablets manufactured by different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable, as the dissolution profile of the products of different manufacturers may not be the same.

For Didanosine Gastro-resistant Capsules

Dissolution (2.5.2).

A. Apparatus No. 2,

Medium. 1000 ml of 0.1 *M hydrochloric acid,*

Speed and time. 100 rpm and 120 minutes.

Determine by liquid chromatography (2.4.14).

Test solution. Dissolve all the granules from the basket in 750 ml of buffer solution pH 7.5 prepared by dissolving 1.41 g of *disodium hydrogen orthophosphate anhydrous* in 900 ml of *water*, adjusted to pH 7.5 with *orthophosphoric acid*, and dilute to 1000 ml with *water*. Dilute suitably to get a solution containing about 0.005 per cent w/v of didanosine in the buffer solution.

Reference solution. A 0.005 per cent w/v solution of *didanosine RS* in the buffer solution.

Chromatographic system

– a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5µm),

– mobile phase: a mixture of 950 volumes of buffer solution pH 7.5 and 50 volumes of *acetonitrile*,

– flow rate: 1.5 ml per minute,

– spectrophotometer set at 249 nm,

– injection volume: 10 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 3000 theoretical plates the tailing factor is not more than 1.5 and the relative standard deviation of replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{10}H_{12}N_4O_3$ released in the acid medium by subtracting the content of $C_{10}H_{12}N_4O_3$ in the test solution from the total content of didanosine, $C_{10}H_{12}N_4O_3$ determined in the Assay.

Complies with the acceptance criteria given under Acid stage.

B. Apparatus No. 2,

Medium. 1000 ml of a buffer solution prepared by mixing 250 ml of *0.2 M tribasic sodium phosphate buffer* and 750 ml of *0.1 M hydrochloric acid* and adjusting the pH to 6.8 with *2 M hydrochloric acid or 2 M sodium hydroxide,*

Speed and time. 100 rpm and 45 minutes.

Run for 120 minutes at 100 rpm using the medium given in method A. At the end of this period discard the medium from each vessel without losing any of the granules and fill the empty vessel with the dissolution medium preheated to 37°. After running the apparatus for 45 minutes. withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute a suitable volume of the filtrate with dissolution medium to obtain 0.005 per cent w/v of didanosine.

Reference solution. A 0.005 per cent w/v solution of *didanosine RS* in the dissolution medium.

Use the chromatographic system described under test A.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 3000 theoretical plates, the tailing factor is not more than 1.5 and the relative standard deviation of replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

D. Not less than 75 per cent of the stated amount of $C_{10}H_{12}N_4O_3$.

6.	Related Substances/ Impurities	Tests for related substances or impurities arising on manufacture or storage of the dosage form shall be included. The tests applied to the bulk drug substance shall be applied, wherever possible with necessary modifications.	**For Chlorthalidone Tablets** **Related substances.** Determine by thin-layer chromatography (2.4.17), coating the plate with *silica gel GF254.* *Mobile phase.* A mixture of 75 volumes of *butanol* and 15 volumes of *1M ammonia.* *Test solution.* Shake a quantity of the powdered tablets containing 50 mg of Chlorthalidone with 5 ml of *acetone*, centrifuge and use the supernatant liquid.

Reference solution. A 0.01 per cent w/v of 2-*(4-chloro-3-sulphamoylbenzoyl) benzoic acid RS* in *acetone.*

Apply to the plate 10 µl of each solution. After development, dry the plate in air and examine under ultraviolet light at 254 nm. Any secondary spot in the chromatogram obtained with the test solution is not more intense than the spot in the chromatogram obtained with the reference solution.

For Citalopram Tablets

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Weigh a quantity of the powdered tablets containing 50.0 mg of citalopram, disperse in 100.0 ml of the mobile phase and filter.

Reference solution (a). A 0.625 µg per ml solution of *citalopram hydrobromide RS* in the mobile phase.

Reference solution (b). A solution containing 0.0001 per cent w/v of *citalopram impurity B RS [[3-(3N,N-dimethylamino)-1-(4-fluorophenyl)-6-c vano-1(3H)-isobenzofuranone]RS]* and 0.025 per cent w/v of *citalopram hydrobromide RS* in the mobile phase.

Chromatographic system

– a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),

– column temperature: 45°,

– mobile phase: a mixture of 55 volumes of a buffer solution prepared by dissolving 3.15 g of *potassium dihydrogen phosphate* and 3.6 g of *disodium hydrogen phosphate* in 1000 ml of *water*, 38 volumes of *methanol* and 7 volumes of *acetonitrile*, adjusted to pH 6.5 with *orthophosphoric acid*,

– flow rate: 0.8 ml per minute,

– spectrophotometer set at 239 nm,

– injection volume: 20 µl.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to citalopram impurity B and citalopram is not less than 3.0.

Inject reference solution (a). The test is not valid unless the column efficiency is not less than 5000 theoretical plates, the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 5.0 per cent.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test

solution, the area of any secondary peak is not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.25 per cent) and the sum of the areas of all the secondary peaks is not more than 8 times the area of the principal peak in the chromatogram obtained with reference solution(a) (0.8 per cent).

7.	Specific Tests	Depending on the dosage form, details of any test parameter and the method of testing for it that is not included in the General Monograph on a Dosage Form, or is specific to a particular dosage form shall be given.	**For Ascorbic Acid Injection** **Oxalic acid.** Dilute a volume containing 0.25 g of Ascorbic Acid in 5 ml of *water* and neutralise to litmus paper with *2 M sodium hydroxide*. Add 1 ml of *2 M acetic acid* and 0.5 ml of *0.5 M calcium chloride*. Any opalescence, after 60 minutes, is not more intense than that produced by treating 5 ml of a solution prepared by dissolving 70 mg of oxalic acid in 500 ml of *water* in a similar manner (0.3 per cent). **For Aspirin Tablets** **Salicylic acid.** To a quantity of the powdered tablets containing 0.5 g of Aspirin add 25.0 ml of *chloroform* shake vigorously for 2 minutes and filter through a dry filter paper. Evaporate 5.0 ml of the filtrate rapidly to dryness in a dish in a current of dry air at room temperature. Dissolve the residue in 2 ml of *ethanol (95 per cent)*, transfer to a Nessler cylinder, using a further 1 ml of *ethanol (95 per cent)* to rinse the dish, dilute to 50 ml with *water*, add 1 ml of *acid ferric ammonium sulphate* solution, mix, and allow to stand for 1 minute; the violet colour produced is not more intense than that produced by adding 1 ml of *acid ferric ammonium sulphate* solution to a mixture of 2.0 ml of a freshly prepared 0.15 per cent w/v solution of salicylic acid, 3 ml of *ethanol (95 per cent)* and sufficient *water* to produce 50 ml contained in a second Nessler cylinder (3 per cent). **For Protamine Sulphate Injection** **Optical rotation** (2.4.22). –0.68° to –0.52°, determined in a solution prepared by diluting the injection with *0.5M hydrochloric acid* so as to contain 0.8 per cent w/v of Protamine Sulphate. **Abnormal toxicity** (2.2.1). Complies with the test for abnormal toxicity, using a volume containing 10 mg of Protamine Sulphate per kg of the rabbit's weight.
8.	Disintegration	**Disintegration.** The time for which the disintegration test apparatus is to be operated is to be given only when it is different from that in the General Monograph on Tablets *Note-* Where the test for disintegration	**For Cyclophosphamide Tablets** **Disintegration** (2.5.1). Not more than 30 minutes. **For Piperazine Phosphate Tablets**

		is not applicable; the following statement shall be included: **Disintegration.** The test for Disintegration does not apply to tablets that are intended to be chewed before swallowing.	**Disintegration.** The test does not apply to Piperazine Phosphate tablets intended to be chewed before swallowing.
9.	Uniformity of content	<u>For Cyclophosphamide Tablets</u> **Uniformity of content** *(for tablets containing 10 mg or less)*. Complies with the test stated under Tablets. Place one tablet in a 10-ml volumetric flask, add about 7 ml of *water*, shake until the tablet is completely disintegrated, dilute with water to volume and filter. Wash the filter quantitatively with 10 ml of *water* and combine the filtrate and washings (test solution). In another volumetric flask dissolve an accurately weighed quantity of *cyclophosphamide RS* in water to obtain a solution of known concentration of about 500 µg per ml (reference solution). Place in separate test-tubes (170 mm x 25 mm) 2.0 ml of the test solution, 2.0 ml of the reference solution and 2.0 ml of water as the blank. Treat each tube in the following manner. Add 0.7 ml of a 2.35 per cent v/v solution of *perchloric acid* in water, mix and heat on a water-bath for 10 minutes. Cool, add 1 ml of *0.1 M sodium acetate* and mix. Add 1.6 ml of a 0.75 per cent w/v solution of *4-(4-nitrobenzyl) pyridine in 1,2-ethanediol,* mix and heat on a water-bath for 10 minutes. Cool, add 8.0 ml of a 2 per cent w/v solution of *sodium hydroxide* in *ethanol (95 per cent).* Measure the absorbances of the solutions against the blank within 4 minutes at the maximum at about 560 nm (2.4.7). Calculate the content of $C_7H_{15}Cl_2N_2O_2P$ in the tablet.	
10.	Other tests	A general statement directing towards General monograph "Tablet" needs to be mentioned.	**Other tests.** Comply with the tests stated under Tablets.
11.	Assay	Assay can be performed as under: <u>By HPLC method</u> **Assay.** Determine by liquid chromatography (2.4.14). *Test solution.* Directions for preparing to be given	<u>For Cyclophosphamide Tablets</u> **Assay.** Weigh and powder 20 tablets. To a quantity of the powder containing 0.1 g of anhydrous cyclophosphamide add 30 ml of *chloroform,* shake vigorously for 15 minutes, filter

		Reference solution.– do – • Chromatographic system: • details of the column, • mobile phase composition and flow rate, • detector and wavelength setting, • injection device (if any), and • any other detail. *Note*- Commas are to be put after each item except the last where a full stop is to be given. Instructions for carrying out the determination, including the volumes to be injected, sequence of injections etc. Calculate the percentage content of xxxx, where xxxx is the chemical entity mentioned in the opening purity statement.	and wash the filter with 15 ml of *chloroform*. Evaporate the combined filtrate and washings to dryness and dissolve the residue in 50 ml of a 0.1 per cent w/v solution of *sodium hydroxide* in *1,2-ethanediol*. Boil the solution under a reflux condenser for 30 minutes, allow to cool and rinse the condenser with 25 ml of *water*. Add 75 ml of *2-propanol,* 15 ml of *2 M nitric acid,* 10 ml of *0.1 M silver nitrate* and 2 ml of *ferric ammonium sulphate solution* and titrate with *0.1 M ammonium thiocyanate.* Carry out a blank titration. 1 ml of *0.1 M silver nitrate* is equivalent to 0.01305 g of $C_7H_{15}Cl_2N_2O_2P$. **For Clozapine Tablets** **Assay.** Determine by liquid

chromatography (2.4.14)

Test solution. Weigh and powder 20 tablets. Weigh a quantity of the powder containing 125 mg of Clozapine, dissolve in 640 ml of *methanol* and add sufficient water to produce 1000 ml.

Reference solution (a). Weigh 12.5 mg of *clozapine RS* in 80 ml of *methanol* and dilute to 100.0 ml with *water*.

Reference solution (b). Weigh accurately about 10 mg of Clozapine, add 5 ml of *0.1 M hydrochloric acid* and heat for 2 hours at 90°. Cool, add 15 ml of *water*, dilute with *methanol* to 100.0 ml and mix. To 10.0 ml of the solution, add 10.0 ml of reference solution (a) and mix.

Chromatographic system

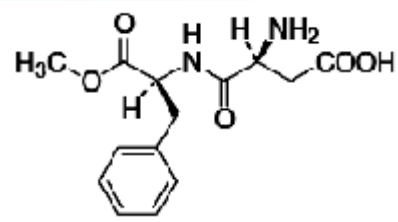
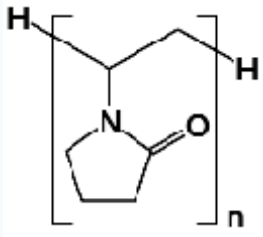
– a stainless steel column 25 cm x 4.0 mm, packed with octylsilane bonded to porous silica (5 µm),

– mobile phase: 800 volumes of *methanol*, 200 volume of *water* and 0.75 volume of *triethylamine*,

		– flow rate: 1 ml per minute, – spectrophotometer set at 257 nm, – injection volume: 10 µl. Inject reference solution (a). The test is not valid unless the column efficiency is not less than 1500 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent. Inject reference solution (b). The resolution between the clozapine peak and any secondary peak is not less than 1.5. Inject reference solution (a) and the test solution. Calculate the content of $C_{18}H_{19}ClN_4$ in the tablets.	
12.	Storage	Directions for storing the product with particular reference to the nature of the pack and storage temperatures (as appropriate) shall be stated.	**Storage.** Store protected from light, at a temperature not exceeding 30°. OR **Storage.** Store protected from light and moisture and against attack by insects and rodents.
13.	Labelling	Any specific requirement relating to the standard of the product or the storage directions shall be given.	**Labelling.** The label states the quantity of the active ingredient in terms of the equivalent amount of amoxicillin. **Labelling.** The label states (1) the number of Units per ml; (2) the species of animal from which the preparation has been made; (3) the name and proportion of any added preservative; (4) that the preparation, if liquid, should not be allowed to freeze; (5) that the preparation, if dried, should be used immediately after reconstitution in the stated quantity of the diluent.

Monograph Development on Inactive Ingredients (Pharmaceutical Aids & Excipients)

MONOGRAPH DEVELOPMENT ON INACTIVE INGREDIENTS (PHARMACEUTICAL AIDS & EXCIPIENTS)

S. No.	Content	Monograph	Example
1.	Title of the Monograph	Name of the item printed in bold letters in Times New Roman font size 14 pt (Times New Roman).	**Aspartame** **Croscarmellose Sodium** **Crospovidone** l-Ethenyl-2-pyrrolidinone homopolymer; 1-Vinyl-2-pyrrolidinone homopolymer
2.	Formula	If applicable to the monographs the representation shall be as under: 1.Structural (Graphic) Formula 2.The molecular formula on the left and the molecular weight expressed to one decimal place on the right, two spaces below the graphic formula	**Aspartame**  **$C_{14}H_{18}N_2O_5$ Mol. Wt. 294.3** **Crospovidone**  **$(C_6H_9NO)n$ Mol. Wt. (111.1)n**
3.	Opening Statement	The statement shall define the article.	Emulsifying Wax is a waxy solid containing 90 parts of Cetostearyl Alcohol, 10 parts of Sodium Lauryl Sulphate or

			sodium salts of similar sulphated higher primary aliphatic alcohols, and 4 parts of Purified Water. Activated Charcoal is obtained from vegetable matter by suitable carbonisation processes intended to confer a high adsorbing power.
4.	Category	Category is to be given as informative part of the drug. Only the category needs to be mentioned	**Croscarmellose Sodium** Category. Excipient
5.	Description, Identification andother tests, including Assay	These shall be expressed in the manner detailed above under Section A. *Note-* In the case of plant materials (not products derived from them), after Description the following shall be added, where applicable: It has (or they have) the macroscopic and microscopic characters described under Identification tests….. Only the category needs to be mentioned	
6.	Relative density	xxx to yyy, at ……°. x and y shall be reported to three decimal places only.zz	**Relative density** (2.4.29). 0.815 to 0.880 at 60°.
7.	Weight per ml	x.xxx to y.yyy X and Y shall be reported to three decimal places	**For Phenylethyl Alcohol Weight per ml** (2.4.29). 1.017 g to 1.02 g. **For Polyoxyl 35 Castor Oil Weight per ml** (2.4.29). 1.05 g to 1.06 g.
8.	Refractive index	x.xxx to y.yyy at …..° . X and Y shall be reported to three decimal places, unless otherwise stated.	**For Phenylethyl Alcohol Refractive index** (2.4.27). 1.531 to 1.534 at 20°.

9.	Melting range	A range is to be provided	**Melting range** (2.4.21). 192° to 195°
10.	Freezing point	xx° to yy°	**For Polyethylene Glycol 1500 Freezing point** (2.4.11). 42° to 46°.
11.	Viscosity	x mPa.s to y mPa.s, at ….°, along with viscometer detail being used.	**Viscosity** (2.4.28). 25 $mm^2s^{-1}$to 32 mm^2s^{-1}, determined at 100° by Method A using a U-tube viscometer (size D). **Viscosity** (2.4.28). 600 to 850 centipoises at 25°, a capillary viscometer being used.
12.	Peroxide value, Acid value, Ester value	Not more than xxx. Result shall be reported to one decimal place only.	**Peroxide value** (2.3.35). Not more than 10.0. **Acid value** (2.3.23). Not more than 8.0, determined on 5.0 g.
13.	Unsaponi-fiable matter Acetyl value, Hydroxyl value, Saponi-fication value	Not less than xxxx. Values shall be rounded to the next higher integer. No decimals to be used.	**Unsaponifiable matter** (2.3.39). Not more than 1.5 per cent. **Acetyl value** (2.3.22). Not less than 143. **Hydroxyl value** (2.3.27). Not less than 150 **Saponification value** (2.3.37). 176 to 187.
14.	Iodine value	xx to yy. Values shall be rounded to the next higher integer. No decimals to be used	**Iodine value** (2.3.28). 82 to 90.
15.	Acidity or alkalinity	Method of preparing the test solution and the indicator to be used to be given. Not more than x ml of yM sodium hydroxide is required to change the colour of the solution.	**Acidity or alkalinity.** To 1.0 g add 10 ml of *ethanol* and 0.1 ml of *phenol red solution*. Not more than ml of 0.01M *sodium hydroxide* is required to change the colour of the solution.

17.	Storage	Special storage conditions, if any shall be specified These shall be expressed in the manner detailed above under Section A.	
18.	Labelling	Any special labelling statements specific to the product and also not stipulated in the Drugs Rules shall be given.	The label states whether it is Sumatra Benzoin or *Siam Benzoin.*

Monograph Development on Herbs, Processed Herbs & Herbal Products

MONOGRAPH DEVELOPMENT ON HERBS, PROCESSED HERBS & HERBAL PRODUCTS

	Monograph	Example
Title of the Monograph	For monographs intended for inclusion in pharmacopoeias, the title of the monograph should be printed in bold letters in Times New Roman font size 14 pt (Times New Roman). It should include the Latin binomial nomenclature or Synonym or Common Name whichever is appropriate and this is followed by the name of plant part(s) or plant material (e.g. resin, gum-resin) and where applicable, its state and type of herbal preparation (e.g. aqueous extract and Non aqueous extract and its dosage form (tablet, capsule, etc.). Subsidiary or abbreviated title or synonym (if any) may be shown two spaces below the main title (in ordinary letters) The main monograph headings viz. Identification and Tests etc. shall be in Times New Roman size 11 pt, and the headings of the individual tests in size 10 pt, and all in bold letters.	**Amaltas** Sonhali; *Cassia fistula* **Belladona Leaf** **Daruharidra Roots** Berberis, *Berberis arisata* **Daruharidra Stems** Berberis; *Berberis aristata* **Mandukaparni Dry Extract** Gotu Kola; *Centella asiatica*
Photograph	**Requirements for inclusion of photograph of an herb /part of the herb** a) An herbal monograph in IP provides photograph of the herb. Such a photograph shall provide a clear visual depiction of the herb, part of the herb. b)A photograph of the herb shall appear immediately after the title/synonym in	

the monograph.

c) An authentic sample of herb/part of a herb, properly cleaned, kept within a grid printed on a paper which gives it the size denotation as illustrated in Table 1 shall be photographed using an appropriate camera with a minimum of 3 megapixels capacity. The pieces should be clearly visible.

d) Alternatively, place such a sample on a glass plate which can be illuminated from below using a suitable lamp and photograph it from a suitable distance from the top with proper focus. While doing so depending on the colour of the backgrounds like butter paper, white paper, black paper etc. may be used suitably.

e) The photograph shall be saved and reproduced in the IP as a composite photograph occupying a size of 8 x 6 cm.

f) Alternatively, the same may also be reproduced in such a way to cover the requisite units occupying 5 x 6 cm and a photograph of 1 or maximum 2 single units in a "close up" mode occupying 3 x 6 cm size. In no case any photograph shall exceed 8 x 6 cm size. (Table 1) Describe the number of units of each material to be taken for the photograph.

Category	No. of Units	Category	No. of Units
Woody and available in large pieces–stem, wood, and heartwood, woody roots (Eg. Deodar, Erandmool)	4-6	Stems and roots with smaller diameters (Eg. Ephedra, Manjistha, Kutaki)	8-14
Leafy and creepers cut into parts (Eg. Bhringraj, Neem)	10- 12	Stigma, Style, Anthers, Small Petals, Buds (Eg.Keshar, Lavang)	20-40
Fleshy Dried Rhizomes (Eg.Vidarikand, Varahi)	4-8	Minute seeds and parts of seeds (Eg.Vakuchi, Isabgol)	More than 40
Flowers, Larger Petals, Small Fruits (Eg.Japakusum, Kusumphool)	10-20	Resins, Gums in dried form (Eg. Heeng, Babool)	4-8
Bark cut into pieces (Eg. Arjuna, Kutaz)	3-8	Minute parts like epidermal hair (Eg. Kamela)	5-10

Table 1: Description of number of units of each herbal material

Grid to be used to place the herbs for photograph (Each block is of 1 cm2)

Definition	**Some or all of the following are usually included in the definition:** • the state of the drug: whole, fragmented, peeled, cut, fresh or dried; • the complete scientific name of the plant (genus, species, subspecies, variety, author); commonly used `synonyms may be mentioned • the part or parts of the plant used • where appropriate, the stage in the growth cycle when harvesting takes place, or other necessary information • wherever possible, the minimum content of quantifiable constituents (either responsible for the biological activity of the herb (bio-marker) or a chemical compound known to be present in the herb even if not	Amaltas consists of dried pulp of fruits of *Cassia fistula* Linn. (Fam. Caesalpiniaceae). Belladonna Leaf consists of the dried leaf and flowering tops of *Atropa belladonna* Linn. or of A. *acuminata* Royle ex Lindley (Fam. Solanaceae) or a mixture of both species. Daruharidra Roots consist of the dried roots of *Berberis aristata* DC (Fam. Berberidaceae). Daruharidra Stems consist of cut dried stems of *Berberis aristata,* DC (Fam. Berberidaceae). Arjuna Dry Extract is obtained by extracting Arjuna *(Terminalia arjuna* Wight and Arn,Fam. Combretaceae) bark with

	responsible for biological activity (chemical/ analytical marker) • Herbal drugs very often contain a mixture of related substances, in which case the total content of quantifiable constituents is determined and expressed as one of the constituents, usually the major constituent; separate limits may be given for different forms of the drug (whole/cut).	*methanol* or any other suitable solvent and evaporation of solvent. Clove Stem Oil is the essential oil obtained by steam distillation from the dried stems of *Syzygium aromaticum* L. Merr. And Perry syn. Eugenia caryophyllus (Sprengel) Bullock and S. Harrison (Fam. Myrtacae).
Statement of Purity	A definitive statement of the purity of the article, two spaces below Chemical name, and expressed in the following manner: AB contains not less than X per cent and not more than Y per cent of the phytochemical constituents, calculated on the dried basis (where a test for loss on drying is specified). Where, AB is the pharmacopoeial name of the article X and Y are the lower and higher percentage figures respectively, expressed to one decimal place only.	Amaltas contains not less than 0.07 per cent w/w of rhein, calculated on the dried basis. Belladonna leaf Herb contains not less than 0.30 per cent of total alkaloids, calculated as hyoscyamine with reference to the material dried at 100° to 105°. Daruharidra Stems contain not less than 0.5 per cent w/w of berberine, calculated on the dried basis. Ashwagandha Dry Extract contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of withaferin A, not less than 85.0 per cent and not more than 110.0 per cent w/w of the total withanolides calculated as the sum of free withanolides and glycowithanolides calculated on the dried basis. The extract also contains not less than 1.0 per cent of alkaloids, calculated on the dried basis. Clove Bud Oil contains not less than 75.0 per cent and not more than 85.0 per cent of eugenol, not less than 8.0 per cent and not more than 15.0 per cent of eugenyl acetate.

Category	Category is to be given as informative part of the drug. Only the category needs to be mentioned.	**Amaltas** **Category.** Purgative, diuretic, antipruritic, febrifuge, vibandha **Belladona Leaf** **Category.** Anticholinergic Daruharidra Roots **Category.** Hepatoprotective, antiinflammatory, anticancer, amatisara. **Castor Oil** **Category.** Irritant puragative, antirheumatic, amavata **Coleus Dry Extract** **Category.** Cardiac stimulant, hypotensive, spasmolytic
Usual Strength	Usual strength needs to be mentioned in case of processed herbs or herbal formulations	**Garcinia Aqueous Extract** **Usual strengths.** 50 per cent; 60 per cent w/w . **Haritaki Extract** **Usual strength.** 15 per cent w/w.
Description	A brief description of the organoleptic characters of the drug such as colour, odour, taste etc.	**Amaltas** **Description.** Pulp is dark brown, sticky, sweet and mucilaginous; odour characteristic, somewhat disagreeable. **Haritaki Extract** **Description.** Light yellowish to yellowish brown powder with odour, characteristic; taste, bitter. **Hydrogenated Castor Oil** **Description.** A white to yellow powder of uniform consistency and texture. It may have a hard, waxy consistency.

Identification	The purpose of this section is to ensure that article under examination is in agreement with what is stated in the Definiton of the article. All the identifications mentioned below are not necessarily included: some may be absent when they are not feasible or are not significant for the purpose of identification. 1) **Macroscopic:** The important macroscopic botanical characteristics of the herbal materials are specified to permit a clear identification. Where two or more species of a genus or subspecies are included in the definition, the differences, if any, between them should be indicated. 2) **Microscopic:** It involves gross microscopic examination of the drug and it can be used to identify the organized/ unorganized drugs by their known histological characters. It is mostly used for qualitative evaluation of organized crude drugs in entire and powder forms with help of microscope. It involves using microscope for detecting various cellular tissues and their arrangements such as trichomes, stomata, starch granules and calcium oxalate crystals etc. Crude drug can also be identified microscopically by cutting the thin TS (transverse section)/ LS (Longitudinal section) especially in case of wood. Quantitative aspects of microscopy include study of stomatal number and index, palisade ratio, vein-islet number, size of starch grains and	**For Daruharidra Roots** *A. Macroscopic* — Root cylindrical, more or less knotty, strongly branched, usually cut into pieces of varying length and up to 45 mm in diameter; externally light yellowish-brown, longitudinally wrinkled and short scaly; fracture hard and tough; bark 1 mm. in thickness, easily separable into layers; wood yellow. *B. Microscopic* — The powder is yellowish-brown; composed chiefly of fragments of wood fibers associated with a few tracheae and medullary rays; wood fibers yellowish, scarcely giving any reaction with *phloroglucinol* and *hydrochloric* acid, and with large, simple, transverse pores; trachea chiefly scalariform with bordered pits, occasionally reticulate; medullary rays one to twelve cells wide, and in very long rows; starch grains simple or two- to three-compound, the individual grains being irregularly spherical. C. Determine by thin-layer chromatography (2.4.17), coating the plate with *silica gel* GF 254. *Mobile phase.* A mixture of 80 volumes of *ethyl acetate,* 10 volumes of *formic acid,* 10 volumes of *glacial acetic* acid and 20 volumes of *water.* *Test solution.* To 2 g of the coarsely powdered substance under examination, add 40 ml of *methanol*, reflux for 15 minutes,

	length of fibers etc. 3)**HPLC/ TLC/ HPTLC/ GC:** The method used must be able to distinguish the material of interest from other materials with potential for species substitution and suspected adulteration. For methods of TLC/HPTLC, description must include color and position of the characteristic bands. A color *image of a*	cool and filter. Reflux the residue further for two times with 25 ml of *methanol,* cool and filter. Combine all the filtrates and concentrate under vacuum to 25 ml. *Reference solution.* To 1 g of the *daruharidra roots RS*, add 40 ml of *methanol,* reflux for 15 minutes, cool and filter. Reflux the residue
	further for two times with 25 ml of methanol, cool and filter. Combine all the filtrates and concentrate under vacuum to 25 ml. Apply to the plate 10 µl of each solution as bands 10 mm by 2 mm. Allow the mobile phase to rise 8 cm. Dry the plate in air and examine under ultraviolet light at 254 nm and 365 nm and also under day light The chromatographic profile of the test solution is similar to that of the reference solution **<u>For Nutmeg Oil</u>** A. Determine by gas chromatography (2.4.13). *Test solution.* A 2.0 per cent w/v solution of the oil under examination in *ethanol (95 per cent)*. Reference solution. A 2.0 per cent w/v solution of nutmeg oil RS in *ethanol* (95 per cent). Use chromatographic system described in the Assay. The peaks in the chromatogram obtained with the test solution correspond to the peaks in the chromatogram obtained with the reference solution. B. Flash point (2.4.44). 46.0º to 50.0º.	
Tests	Depending on the article few tests may be omitted or specific tests other than this may be performed.	
	Raw Herb- 1) Foreign Organic Matter: 2) Ethanol soluble extractive 3) Water-soluble extractive 4) Total ash 5) Acid-insoluble ash	6) Heavy metals 7) Loss on Drying 8) Microbial contamination **Processed Herbs/ Pharmaceutical aids/ Formulations-** 1) Water-soluble extractive

	2) Ethanol soluble extractive 3) Acid-insoluble ash 4) Total ash 5) Water/ Loss on drying 6) Heavy metals 7) Microbial contamination 8) Disintegration (in case of tablets) **Essential Oil-** 1) Weigh per ml 2) Refractive Index 3) Relative density	4) Optical Rotation 5) Alkaline impurities 6) Semi-drying oil 7) Peroxide Value 8) Acid value 9) Acetyl value 10) Hydroxyl Value 11) Iodine value 12) Saponification value 13) Rancidity 14) Unsaponifiable matter 15) Heavy metal 16) Water
Foreign Organic Matter	Generally a limit of 2% of foreign matter is imposed, unless otherwise prescribed in a specific monograph. Where a limit for foreign matter greater than 2% is to be prescribed, it is stated in the specific monograph with an indication of the type of foreign matter. Where necessary, the monograph should indicate how the foreign matter is identified	**Amaltas** **Foreign organic matter** (2.6.1). Not more than 2.0 per cent. **Belladona Leaf** **Foreign organic matter** (2.6.1). Not more than 3 per cent. **Garcinia** **Foreign organic matter** (2.6.1). Not more than 5.0 per cent.
Ethanol soluble/ water soluble extractive	This method determines the amount of active constituents extracted with solvents from a given amount of herbal material	**Amaltas** **Ethanol-soluble extractive** (2.6.2). Not less than 8.0 per cent. **Water-soluble extractive** (2.6.3). Not less than 41.0 percent by method I.
Total ash/ Acid-insoluble ash/ Water-soluble ash	The *total ash* method is designed to measure the total amount of material remaining after ignition. *Acid-insoluble ash* measures the amount of silica present, especially as sand and siliceous earth	**Amaltas** **Total ash** (2.3.19). Not more than 18.0 per cent. **Acid-insoluble ash** (2.3.19). Not more than 1.3 per cent.

Heavy metals	Usually 1g of material is taken unless otherwise justified.	**Amaltas** **Heavy metals** (2.3.13).1.0 g complies with the limit test for heavy metals, Method B (20 ppm).
Loss on drying	It is the loss of weight expressed as percentage w/w resulting from water and volatile matter of any kind that can be driven off under specified conditions.	**Amaltas** **Loss on drying** (2.4.19). Not more than 6.2 per cent, determined on 5 g by drying in an oven at 105°.
Microbial Contamination	The monographs should refer to the General chapter 2.2.9 with a statement that it complies with the microbial contamination tests.	**Amaltas** **Microbial contamination** (2.2.9). Complies with the microbial contamination tests.
Weight per ml	x.xxx to y.yyy where-X and Y shall be reported to three decimal places	**Peppermint Oil** **Weight per ml** (2.4.29). 0.900 g to 0.916 g.
Refractive index	x.xxx to y.yyy . where- X and Y shall be reported to three decimal places, unless otherwise stated.	**Castor Oil** **Refractive index** (2.4.27). 1.4758 to 1.4798. **Nutmeg Oil** **Refractive index** (2.4.27). 1.475 to 1.485.
Relative density	xxx to yyy, at ……°. x and y shall be reported to three decimal places only.	**Peppermint Oil** **Relative Density** (2.4.29). 0.890 to 0.910.
Optical Rotation	+x.x°to +x.x°or –y.y°to -y.y°. The method of preparing the test solution may be given in some cases. Results to be reported to only one decimal place.	**Castor Oil** **Optical rotation** (2.4.22). +3.5° to +6.0°.
Acid value, Acetyl value, Hydroxyl Value, Iodine value, Saponification value	**Castor Oil** **Acid value** (2.3.23). Not more than 2.0. **Acetyl value** (2.3.22). Not less than 143. **Hydroxyl value** (2.3.27). Not less than 150. **Saponification value** (2.3.37). 176 to 187. **Iodine value** (2.3.28). 82 to 90.	

<table>
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<td>Assay</td>
<td>Assay can be performed as under:

<u>By TLC</u>

Assay. Determine by thin-layer chromatography (2.4.17), coating the plate with silica gel GF254.

By HPLC method

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Directions for preparing to be given
Reference solution. – do –
Chromatographic system:
• details of the column,
• mobile phase composition and flow rate,
• detector and wavelength setting,
• injection device (if any), and
• any other detail.

Note- Commas are to be put after each item except the last where a full stop is to be given.

Instructions for carrying out the determination, including the volumes to be injected, sequence of injections etc.

Calculate the percentage content of xxxx, where xxxx is the phytochemical constituent mentioned in the opening purity statement.

<u>By Gas Chromatography</u>

Assay. Determine by gas chromatography (2.4.13) (refer identification section)</td>
<td>Amaltas

Determine by thin-layer chromatography (2.4.17),

coating the plate with silica gel GF254.

Mobile phase. A mixture of 3 volumes of toluene, 3 volumes of ethyl acetate, 0.8 volumes of formic acid and 0.2 volumes of methanol.

Test solution. Reflux 1 g of coarsely powdered substance under examination three times with 25 ml of 0.01 M methanolic potassium hydroxide solution for 30 minutes, cool and filter. Combine the filtrates and evaporate to dryness. Dissolve the residue in methanol and dilute to 25 ml with methanol.

Reference solution. Reflux 1 g of amaltas RS with 25 ml of 0.01 M methanolic potassium hydroxide for 1 hour on water bath. Cool and filter. Extract three times with 25 ml of diethyl ether. Combine all the extracts and concentrate under vacuum to dryness. Dissolve the residue in 25 ml of methanol.

Apply to the plate 10µl of each solution as bands 10 mm by 2 mm. Allow the mobile phase to</td>
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<td colspan="2">rise 8 cm. Dry the plate in air and scan the plate in air examine in the ultraviolet light at 366 nm. The chromatographic profile of the test solution is similar to that of the reference solution. absorbance mode at 434 nm. Record the chromatograms and measure the responses for the analyte peak.</td>
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	Arjuna Dry Extract **Assay.** Determine by liquid chromatography (2.4.14). *Test solution.* Shake a quantity of the extract under examination containing about 50 mg of *arjunolic* acid in 50.0 ml of the *methanol,* filter. *Reference solution.* A 0.1 per cent w/v solution of *arjunolic* acid RS in *methanol.* Chromatographic system – a stainless steel column 25 cm x 4.6 mm packed with octadecylsilane bonded to porous silica (5 µm), – mobile phase: a mixture of 35 volumes of 5 mM *cyclodextrin* and 65 volumes of *methanol*, – flow rate: 1 ml per minute, – spectrophotometer set at 205 nm, – injection volume: 20 µl. Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent. Inject the reference solution and the test solution. Calculate the content of the arjunolic acid in the extract.	
Storage	Directions for storing the product with particular reference to the nature of the pack and storage temperatures (as appropriate) shall be stated.	**Storage.** Store protected from heat, moisture and against attack by insects and rodents. OR Storage. Store protected from heat and moisture. OR Storage. Store protected from light at a temperature not exceeding 30°.
Labelling	Any specific requirement relating to the standard of the product or the storage directions shall be given.	Labelling. The label states the strength in terms of the equivalent amount of gugulsterones (Z and E).
HPLC/ GC Chromatogram	a) A HPLC/GC Chromatograms if present shall be incorporated in Volume I of IP. b) Separate chromatogram for the Phytochemical Reference Substances (PRS) and sample under examination should be provided. c) The peak of the PRS/ compound under examination shall be labelled	

	accordingly in the respective chromatograms. Other peaks that may appear in the chromatogram, whose chemical identity is not known, need not be labeled. d) While supplying such HPLC/GC chromatograms please ensure that the chromatogram should; comtlies with; • Contain appropriate scale in X and Y axis with respective units. • Not contain any notations given by the equipments like date, sample details, annotation and all such other matter. • Not contain names of analyst, firms that may appear as a routine part due to settings
TLC chromatogram	a) A "Typical TLC/HPTLC profile" depicts the results of the test for identification/assay used. b) Identification tests by TLC/HPTLC shall be performed as per specification given in the respective monograph.
	a) A "Typical TLC/HPTLC profile" depicts the results of the test for identification/assay used. b) Identification tests by TLC/HPTLC shall be performed as per specification given in the respective monograph. c) As a common practice, the plate shall be of at least 5 cm width and 10 cm height. In this dimension 2 bands each of 10 mm width would be spotted. d) As a rule the extreme left track (track 1) shall always be a Botanical Reference Substance (BRS)/ Phytochemical Reference Substance (PRS). The track 2 of 10 mm width band shall be of a solution of material under examination. e) All the bands shall be applied at a height of 20 mm from the base of the plate. f) During development, the solvent front shall be allowed to move to at 80% of the plate height. g) A photo-documentation of the plate developed as above, after visualization under UV 254 nm and 365 nm, and/or by any derivitizing or by spraying reagents shall be photographed.

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