भारतीय भेषज संहिता आयोग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय, भारत सरकार
सैक्टर २३, राज नगर
गाज़ियाबाद २०१००२ (उ. प्र.), भारत

INDIAN PHARMACOPOEIA COMMISSION
Ministry of Health & Family Welfare, Government of India
Sector 23, Raj Nagar
Ghaziabad 201002 (U.P.), INDIA

डा. राजीव सिंह रघुवंशी
सचिव-सह-वैज्ञानिक निदेशक

Dr. Rajeev Singh Raghuvanshi
Secretary-cum-Scientific Director

F. No. T.11015/01/2020-AR&D

Date: 28th November, 2022

To,

1. The Drugs Controller General (India)
2. CDSCO Zonal Offices
3. All State Drug Controllers
4. Members of the Scientific Body of IPC
5. Members of Expert Working Group of the Scientific Body of IPC
6. Directors of Drugs Testing Laboratories
7. Government Analysts
8. IDMA/OPPI/BDMA/FOPE/FSSAI/Small Scale Industry Associations

Subject: Amendment List 01 to IP 2022

The 9th Edition of Indian Pharmacopoeia (IP) 2022 has been released on 1st July, 2022 and will become effective from 1st December, 2022. Based on scientific inputs, some IP monographs of IP 2022 need amendments before their implementation. Accordingly, Amendment List 01 to IP 2022 is being issued containing such amendments and this will become effective from 1st December, 2022.

All concerned are requested to bring it to the notice of all authorities under their control for compliance with the IP 2022.

(Dr. Rajeev Singh Raghuvanshi)
Secretary-cum-Scientific Director

Encl. Amendment List 01 to IP 2022

Final

Amendment List 01 to IP-2022

4.1 Buffer Solutions. Page 1065

Phosphate Buffer pH 7.5, 0.2 M

Line 3

Change **from** : 0.3 per cent w/v

to : 30 per cent w/v

Page 1089

Insert before **Electrolyte reagent for the determination of water**

Edetic Acid; (Ethylenedinitrilo) tetra-acetic acid: $C_{10}H_{16}N_2O_8$= 292.24

Analytical reagent grade of commerce. Chelating and/or complexing agent.

White, crystalline powder. Melts above 220°, with decomposition. Soluble in solutions of alkali hydroxides; very slightly soluble in *water*.

Page 1112

Insert before **Polyoxyethylene 23 Lauryl Ether**

Polyoxyethylene 10 Lauryl Ether: Decaethylene Glycol Monododecyl Ether: $C_{32}H_{66}O_{11}$= 626.86

General laboratory reagent grade of commerce.

Capsules. Page 1297

Gastro-resistant Capsules, Disintegration, line 7

Change **from** : *mixed phosphate buffer pH 6.8*

to : *phosphate buffer pH 6.8*

Glacial Acetic Acid. Page 1374

Identification. B, line 2

Change **from** : reaction (C) of acetates (2.3.1)

to : reaction (B) of acetates (2.3.1)

Amiloride and Hydrochlorothiazide Tablets. Page 1429

Uniformity of content.

Test solution. Last line

Change **from** : amiloride.

to : amiloride hydrochloride.

Insert at the end

Inject reference solution (b) and the test solution.

Calculate the content of $C_6H_8ClN_7O$, HCl in the tablet.

Aminophylline. Page 1434

Assay. *Reference solution (b)*, line 2

Change **from** : *theobromine*

to : *theobromine impurity IPRS*

Aminophylline Injection. Page 1435

Assay. *Reference solution (b)*, line 2

Change **from** : *theobromine*

to : *theobromine impurity IPRS*

Apremilast Tablets. Page 1491

Dissolution. Line 3

Change **from** : 100 ml

to : 1000 ml

Chromatographic system. Lines 3 to 5

Change **to**: mobile phase: mixture of 1000 volumes of *acetonitrile*, 1000 volumes of *water* and 1 volume of *trifluoro acetic acid*,

Azelastine Hydrochloride. Page 1551

Assay. Last line

Change **from** : $C_{22}H_{25}ClN_3O$.

to : $C_{22}H_{24}ClN_3O$, HCl.

Bacitracin Zinc. Page 1571

Zinc. Line 3

Change **from** : Add 50 ml of *xylenol orange triturate*

to : Add 50 ml of *water*, 50 mg of *xylenol orange triturate*

Bisoprolol Fumarate. Page 1646

Optical rotation. Line 1

Change **from** : **Optical rotation** (2.4.22)

to : **Specific optical rotation** (2.4.22)

Carbomers. Page 1741

Benzene. Chromatographic system, line 6

Change **from** : flow rate: 30 ml per minute using nitrogen as the carrier gas.

to : linear velocity: 35 cm per second using nitrogen as carrier gas.

Clemastine Tablets. Page 1903

Dissolution. Para 2, line 8

Change **from** : $C_{21}H_{26}ClNO,C_4H_4O_4$

to : $C_{21}H_{26}ClNO$

Last line

Change **from** : $C_{21}H_{26}ClNO,C_4H_4O_4$

to : $C_{21}H_{26}ClNO$

Clindamycin Palmitate Hydrochloride.

Page 1907

Assay. Last line

Change **from** : Calculate the content of $C_{34}H_{63}ClN_2O_6S$.

to : Calculate the content of $C_{18}H_{33}ClN_2O_5S$.

Clindamycin Phosphate. Page 1909

Identification. Para 1

Change **from** : *Tests B, C and D may be omitted if tests A and D are carried out. Tests A and D may be omitted if tests B, C and D are carried out.*

to : *Tests B and C may be omitted if tests A and D are carried out. Test A may be omitted if tests B, C and D are carried out.*

Clotrimazole Cream. Page 1937

Identification. A, line 3

Change **from** : reference solution

to : reference solution (a)

Assay. After chromatographic system, para 2

Change **to**: Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to clotrimazole and 2-chlorotritanol is not less than 2.0 in the chromatogram obtained with reference solution (b) and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a).

Codeine Phosphate. Page 1945

Identification. F

Change **to**: F. A 4.0 per cent w/v solution gives reaction (A) of phosphates (2.3.1).

Croscarmellose Sodium. Page 1965

Identification. C

Change **to**: C. A 5 per cent w/v solution in *water* gives reaction (a) of sodium salts (2.3.1).

Cyclobenzaprine Hydrochloride. Page 1972

Insert before **Identification**

Description. A white to off-white, crystalline powder.

Related substances. Last para, line 4 and 5

Delete "the area of the peak due to cyclobenzaprine,"

Docusate Sodium. Page 2154

Assay. Last para

Change **to**: 1 ml of *0.5 M alcoholic potassium hydroxide* is equivalent to 0.1112 g of $C_{20}H_{37}NaO_7S$.

Eberconazole Nitrate. Page 2213

Imidazole. *Test solution*, line 2

Change **from** : the mobile phase.

to : *methanol.*

Finasteride Tablets. Page 2357

Dissolution.

Reference solution. Line 3

Change **from** : the same mixture

to : *water*

Histamine Phosphate. Page 2517

Identification. D

Change **to:** D. A 10.0 per cent w/v solution gives reaction (A) of phosphates (2.3.1).

Imatinib Mesylate. Page 2586

Related substances. Chromatographic system

Insert before gradient program

– spectrophotometer set at 267 nm,

Itraconazole. Page 2653

Related substances. *Reference solution (b)*

Change **from:** Dissolve 10 mg of *itraconazole system suitability IPRS* (containing impurities B, C, D, E, F and G) in 1.0 ml of *methanolic hydrochloric acid.*

to: A solution containing 1.0 per cent w/v of *itraconazole IPRS* and 0.001 per cent w/v of *itraconazole impurity F IPRS* in *methanolic hydrochloric acid.*

Lenvatinib Mesylate. Page 2720

Related substances. *Solvent mixture (a)*

Change **from:** Equal volumes of *methanol* and *water.*

to: A 0.05 per cent w/v solution of *ammonium acetate* in a mixture of 50 volumes of *acetonitrile* and 50 volumes of *water.*

Solvent mixture (b).

Change **from:** 70 volumes of *methanol* and 30 volumes of *water.*

to: A 0.05 per cent w/v solution of *ammonium acetate* in a mixture of 25 volumes of *acetonitrile* and 75 volumes of *water.*

Last para

Change **to:** Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to descyclopropyl lenvatinib is not more than 1.45 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.29 per cent), the area of any peak corresponding to methyl analogue of lenvatinib, lenvatinib carboxylic acid, carbamate derivative of APQC, carbamoyl derivative of lenvatinib and nitrile analogue of lenvatinib, each of, is not more than 0.75 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.15 per cent), the area of any other secondary peaks is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent) and the sum of areas of all the secondary peaks is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent). Ignore any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Lenvatinib Capsules. Page 2722

Related substances. *Test solution,* line 4 and 5

Change **from** : mix and filter.

to : centrifuge a portion of the solution, filter.

Uniformity of content. *Test solution*

Insert at the end

Centrifuge a portion of the solution, filter.

Assay. *Test solution*

Change **to:** *Test solution.* Disperse a suitable quantity of intact capsules (not less than 10) in solvent mixture (a) (50 per cent of final volume), with the aid of magnetic stirrer for 20 minutes, add solvent mixture (b) (25 per cent of the final volume), sonicate for 10 minutes with intermittent shaking and dilute to final volume with solvent mixture (b). Dilute a suitable volume of the solution with solvent mixture (c) to obtain a solution containing 0.004 per cent w/v of Lenvatinib. Centrifuge a portion of the solution, filter.

Levamisole Tablets. Page 2728

Dissolution. Line 9

Change **from** : *levamisole IPRS*

to : *levamisole hydrochloride IPRS*

Levetiracetam. Page 2729

Enantiomeric purity. Chromatographic system, line 3

Change **from** : 5 µm

to : 10 µm

Levetiracetam impurity B. *Reference solution (a)*, line 2

Change **from** : *levetiracetam impurity B IPRS*

to : *(S)-2-aminobutanamide hydrochloride (levetiracetam impurity B) IPRS.*

Levocetirizine Tablets. Page 2735

Related substances.

Insert at the end

Ignore any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent).

Lindane. Page 2769

Assay. Last para, line 1

Change **from** : 0.009649

to : 0.009694

Mefloquine Tablets. Page 2842

Identification. A. *Reference solution*, line 1

Change **from** : *mefloquine IPRS*

to : *mefloquine hydrochloride IPRS*

Insert at the end

Labelling. The label states the strength in terms of the equivalent amount of mefloquine.

Nitrofurantoin Tablets. Page 3074

Insert before **Assay**

Other tests. Comply with the tests stated under Tablets.

Paracetamol Infusion. Page 3194

Related substances. Last para, lines 6 to 9

Change **from** : the area of any peak corresponding to 4-chloroacetanilide is not more than 0.001 times the area of the principal peak in the chromatogram obtained with reference solution (a) (10 ppm).

to : the area of any peak corresponding to 4-chloroacetanilide is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (10 ppm).

White Soft Paraffin. Page 3201

Melting range.

Change **from** : 38° to 56°,

to : 38° to 60°,

Perphenazine Tablets. Page 3236

Uniformity of content. Para 2, line 1

Change **from** : $C_{21}H_{26}N_3OS$

to : $C_{21}H_{26}ClN_3OS$

Assay. Para 2, line 1

Change **from** : $C_{21}H_{26}N_3OS$

to : $C_{21}H_{26}ClN_3OS$

Phenylephrine Eye Drops. Page 3256

Related substances.

Reference solution (a). Change **to:**

Reference solution (a). Dilute 1 volume of the test solution to 40 volumes with *methanol.*

Reference solution (b). Change **to:**

Reference solution (b). Dilute 1 volume of the test solution to 100 volumes with *methanol.*

Piperazine Phosphate. Page 3291

Identification. C

Change **to:** C. A 5.0 per cent w/v solution gives reactions of phosphates (2.3.1).

Propylparaben. Page 3385

Para 1

Change **from** : Propylparaben contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{10}H_{12}O_3$, calculated on the dried basis.

to : Propylparaben contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{10}H_{12}O_3$.

Quinapril Hydrochloride. Page 3413

Identification

Insert before A.

Test A may be omitted if tests B and C are carried out. Test B may be omitted if tests A and C are carried out.

Insert at the end

C. It gives the reactions of chlorides (2.3.1).

Rabeprazole Injection. Page 3439

Para 5, line 3

Change **from** : $C_{18}H_{21}N_3O_3SNa$.

to : $C_{18}H_{20}N_3O_3S,Na$

Assay. Last line

Change **from** : $C_{18}H_{21}N_3O_3SNa$.

to : $C_{18}H_{20}N_3O_3S,Na$

Racecadotril. Page 3444

Related substances.

Reference solution (b). Change **to:**

Reference solution (b). A 0.2 per cent w/v solution of *racecadotril impurity A IPRS* in *acetonitrile.* Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the solvent mixture.

Salicylic Acid Ointment. Page 3556

Assay. Line 1

Change **from** : Weigh 10 g and dissolve

to : Disperse a quantity of the ointment containing 200 mg of Salicylic Acid

Silver Sulphadiazine. Page 3581

Related substances. Last para, line 9

Change **from** : sum of areas of all peak

to : area of any other secondary peak

Sitagliptin Phosphate. Page 3587

Identification. C

Change to: C. A 4.0 per cent w/v solution gives reaction (A) of phosphates (2.3.1).

Sofosbuvir. Page 3635

Related substances. Last para, line 10

Change **from** : sum of areas of all peak

to : area of any other secondary peak

Tacrolimus Capsules. Page 3703

Dissolution. Chromatographic system, line 6

Change **from** : *tert-butyl ether*

to : *tert-butyl methyl ether*

Triamcinolone. Page 3854

Related substances.

Test solution. Change **to:**

Test solution. Dissolve 25 mg of the substance under examination in 6 ml of *methanol* and dilute to 10.0 ml with *water.*

Reference solution. Change **to:**

Reference solution. Dilute 1.0 ml of the test solution to 100.0 ml with a mixture of 60 volumes of *methanol* and 40 volumes of *water.*

VITAMINS, MINERALS, AMINO ACIDS, FATTY ACIDS ETC.

Activated Charcoal. Page 4850

Adsorbing power. Line 10

Change **from** : (*a* ml)

to : (*b* ml)

Line 12

Change **from** : (*b* ml)

to : (*a* ml)

Folic acid and Methylcobalamin Tablets. Page 4083

Dissolution. Chromatographic system, line 5

Change **from** : *sulphonate sodium salt*

to : *1-hexane sulphonic acid (sodium salt)*

VACCINES AND IMMUNOSERA FOR HUMAN USE

General Requirements Vaccines for Human Use. Page. 4327

Tests

Insert before **Storage**

Extractable volume. For vaccines labelled to be administered in low volumes like 0.05 ml or 0.1 ml (e.g. BCG Vaccine), select one container and take up individually each dose in a dry syringe of a capacity suitable to measure and administer low volumes like 0.05 ml or 0.1 ml and fitted with a needle of appropriate gauge and length, using the same number of separate syringe assemblies as the number of doses specified. The volume is such that each syringe delivers not less than the stated quantity and container not less than the stated number of doses.

BLOOD AND BLOOD-RELATED PRODUCTS

Anti-A Blood Grouping Serum. Page 4499

Tests

Intensity. Change from:

Type of Reagent	*Test Red Blood Cells*	*Intensity*
Anti-A (Monoclonal)	A_1	3+
	A_2	2+ to 3+
	A_2B	3+ to 4+

to:

Type of Reagent	*Test Red Blood Cells*	*Intensity*
Anti-A (Monoclonal)	A_1	≥ 3+
	A_2	≥ 2+
	A_2B	≥ 3+

Anti-Human Globulin (AHG) Serum. Page 4509

Tests

Potency. Change from:

Type of Reagent	*Test Red Blood Cells*	*Potency*	
		Anti-D IgG	*Anti C3d*
Anti Human Globulin	O +ve (R_1r or R_1R_2)	1: ≥ 32	1: ≥ 4

to:

Type of Reagent	*Test Red Blood Cells*	*Potency*	
Anti Human Globulin	Sensitized O +ve (R_1r or R_1R_2)-C3d	Anti C3d	1: ≥ 4
	Sensitized O +ve (R_1r or R_1R_2)-IgG	Anti-D IgG	1: ≥ 32

Dried Human Antihaemophilic Fraction. Page. 4528

Tests

Haemagglutinins, anti-A and anti-B.

Para *2*

Insert following at the end

'... and haemolysis should not be observed in any of the tube'

Fibrin sealant Kit. Page 4533

For component 2 (Thrombin preparation)

Tests

Assay

Thrombin

Change **from** : The estimated activity is not less than 80.0 per cent and not more than 125.0 per cent of the activity stated on the label.

to : The estimated activity is not less than 80 per cent and not more than 125 per cent of the activity stated on the label. For a component with a low thrombin conc. and a nominal value of approximately 4 IU/ml, the estimated activity is not less than 50 per cent and not more than 150 per cent of the activity stated on the label. The confidence limits (P = 0.95) are not less than 80 per cent and not more than 125 per cent of the estimated activity.

Human coagulation factor VIII (rDNA). Page. 4539

Assay

Change **from**: Determine the assay of human coagulation factor VIII (2.8.6).

The estimated potency is not less than 80.0 per cent and not more than 125.0 per cent of the stated potency. The confidence limits (P = 0.95) are not less than 80.0 per cent and not more than 120.0 per cent of the estimated potency.

to: "Determine the assay of human coagulation factor VIII (2.8.7) or using Assay method-C of Anti-haemophilic fraction monograph.

The estimated potency is not less than 80.0 per cent and not more than 125.0 per cent of the stated potency. The confidence limits (P = 0.95) are not less than 80.0 per cent and not more than 120.0 per cent of the estimated potency."

Human Normal Immunoglobulin for Intravenous use. Page 4544

Tests

Test for anticomplementary activity of immunoglobulin

Insert following at the end

"or by other suitable validated method; where other methods are used, production and test consistency over time are monitored via suitable indicators and by carrying out testing by existing IP method periodically as approved by National Regulatory Authority".

Tests

Anti-A and anti-B haemagglutinins

Para 2

Insert following at the end

'... and haemolysis should not be observed in any of the tube'

BIOTECHNOLOGY DERIVED THERAPEUTIC PRODUCTS

Erythropoietin Concentrated Solution.

Page 4588

Identification F. Determine by N-terminal sequence analysis

Insert following:

NOTE — The test may be omitted for routine lot release once the consistency in production stage has been well established to the satisfaction of the National Regulatory Authority.

Insulin Aspart. Page 4628

Tests

Impurities with molecular masses greater than that of insulin aspart.

Change **from** : *Test solution*. Dissolve 0.4 mg of the substance under examination in 100 ml of *0.01 M hydrochloric acid*. Maintain the solution at 2° to 8° and use within 48 hours.

to : *Test solution*. Dissolve 4.0 mg of the substance under examination in 100 ml of *0.01 M hydrochloric acid*. Maintain the solution at 2° to 8° and use within 48 hours.

Insulin Glargine Injection. Page 4644

Tests

Total Zinc.

Change **from** : **Total Zinc**. Not less than 27 µg per 100 units and not more than 33 µg per 100 units of insulin glargine, determined by atomic absorption spectrometry (2.4.2) as stated under Insulin Preparations.

to : **Total Zinc**. Not less than 20 µg per 100 units and not more than 40 µg per 100 units of insulin glargine, determined by atomic absorption spectrometry (2.4.2) as stated under Insulin Preparations.

VETERINARY PRODUCTS

Buserelin Injection. Page 4844

Insert follwing at the end

Labelling. The label states (1) the strength in terms of the equivalent amount of buserelin in a suitable dose volume; (2) the proportion of Benzyl alcohol; (3) that the contents are meant for veterinary use only; (4) withdrawal period for meat and milk

Storage. Store at room temperature, protected from light

Calcium Borogluconate Injection.

Page 4844

Usual strength.

Change **from** : 25 per cent w/v solution equivalent to 1.9 per cent w/v of calcium (approximately).

to : Equivalent to 2.23 per cent w/v of calcium.

Isoflupredone Acetate Injectable Suspension. Page 4886

Assay. Chromatographic system, lines 1 to 3

Change **from** : – a stainless steel column 30 cm x 4.6 mm, packed with octadecylsilane bonded to porous micro silica particles (1.5 to 10 µm),

to : – a stainless steel column 30 cm x 4 mm, packed with porous silica particles or superficially porous particles (1.5 to 10 µm) (Such as MicroPorasil),

Nandrolone Laurate. Page 4904

Identification. B.

Test solution. Change **to**:

Test solution. Dissolve 0.5 g of the substance under examination in *dichloromethane* and dilute to 100.0 ml with *dichloromethane.*

Nandrolone. *Test solution.* Change **to**:

Test solution. Dissolve 1.5 g of the substance under examination in *dichloromethane* and dilute to 100.0 ml with *dichloromethane.*

Blackquarter Vaccine. Page 4952

Manufacturer's test

Safety and potency.

Change **from** : challenge all vaccinated guinea-pigs along with 2 controls by intramuscular route with 20 viable spores of virulent *C. chauvoei in* saline suspension containing 2 per cent calcium chloride.

to : Challenge all vaccinated guinea-pigs along with 2 controls by intramuscular route with 20 viable spores or with 1 MLD (Minimal Lethal Dose) of virulent *C. chauvoei* in saline suspension containing 2 per cent calcium chloride.