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INDIAN PHARMACOPOEIA COMMISSION
MIN. OF HEALTH & FAMILY WELFARE
GOVERNMENT OF INDIA
SECTOR -23, RAJ NAGAR, GHAZIABAD - 201002

No. IPC/7021/IP-2014/AL-005 **Dated**: 16-12-2016

To,

1. **DCG (I)/ CDSCO, Zonal Offices**
2. **All State Drug Controllers**
3. **Members of Scientific Body of the IPC**
4. **Members of Sub-committee of Scientific Body of the IPC**
5. **Government Analysts**
6. **Director of Drug Laboratories**
7. **IDMA/OPPI/BDMA/FSSAI/Small Scale Industry Associations**

AMENDMENT LIST – 005 for IP 2014

As you are aware that the 7th edition of Indian Pharmacopoeia has become official from 1st April, 2014. Based on scientific inputs, some monographs, appendices needed upgradation, accordingly an Amendment list – 005 is issued containing amendment and upgradation. This is for notice and immediate compliance.

Yours faithfully,

(Dr. G. N. Singh)
Secretary-cum-Scientific Director

Encl:
Amendment List – 005 for IP 2014

CC to: Publication Division to put up on IPC website.

Amendment List-005 to IP-2014

2.2.11. Sterility. Page 59

Method A- Membrane Filtration
Apparatus

Insert at the end.

"Alternatively, an apparatus can be designed so that the solution to be examined can be introduced and filtered under aseptic conditions. It permits the aseptic removal of the membrane for transfer to the medium, or it is suitable for carrying out the incubation after adding the medium to the apparatus itself".

2.4.13. Gas Chromatography. Page 149

Adjustment of chromatographic conditions.
Change **from:** *Injection volume***:** May be decreased provided detection and repeatability of the peak(s) to be determined are satisfactory. No increase is permitted.

to:*Injection Volume and Split Volume***:** The injection volume and split volume may be adjusted if detection and repeatability are satisfactory.

2.4.14. Liquid Chromatography.Page. 152

Adjustment of chromatographic conditions.*Injection volume*
Change **from:** May be decreased provided detection and repeatability of the peak(s) to be determined are satisfactory. No increase is permitted.

to: May be adjusted as far as it is consistent with accepted precision, linearity, and detection limits. Note that excessive injection volume can lead to unacceptable band broadening, causing a reduction in column efficiency and resolution. Applies to both gradient and isocratic separations.

4.1 Buffer Solutions. Page 760

Add after Phosphate Buffer pH 3.0

Phosphate buffer pH 3.0, 0.1 M. Dissolve 12.0 g of *anhydrous sodium dihydrogen phosphate* in *water*, adjust the pH with *dilute phosphoric acid* and dilute to 1000 ml with *water*.

5.8 Dimension of Hard Gelatin Capsule Shells. Page 885

Change **to:**

5.8.1 Dimensions of Hard Gelatin Capsule Shells

Hard Gelatin Capsule Shells normally used for the incorporation of medicaments are cylindrical in shape but other shapes are also formed for special requirements. The shells of the capsules consist of two prefabricated cylindrical sections, one end of which is rounded and the other is open. The shells are of various sizes, usually designated by different numbers, 5 being the smallest and 000 the largest. The dimensions of hard gelatin capsule shells tend to vary with the content of moisture in them and the conditions under which they are stored or to which they are exposed. The chemical composition of the shells also influence the extent to which exposure to heat and moisture affects the dimensions.Nevertheless, the average conventional dimensions (outside diameter, length and wall thickness – single / double) of the capsule shells of sizes 000 to 5 are provided in the table 1, 2 & 3 for the guidance of users. It should be noted that any measurement of reasonable accuracy can be made only under controlled conditions of temperature and humidity. A temperature between 23°and 27°and a relative humidity between 45 per cent and 55 per cent are recommended.

Table 1- Average Outside Diameter		
Size	**Cap (mm)**	**Body (mm)**
000	9.89 – 10.01	9.54 – 9.66
00	8.49 – 8.61	8.16 – 8.28
0	7.60 – 7.72	7.28 – 7.40
1	6.87 – 6.99	6.57 – 6.69
2	6.31– 6.43	6.02 – 6.14
3	5.77 – 5.89	5.50 – 5.62
4	5.27 – 5.39	5.01 – 5.13
5	4.85 – 4.97	4.59 – 4.71

Table 2- Average Length		
Size	**Cap (mm)**	**Body (mm)**
000	12.5 – 13.5	21.7 – 22.7
00	11.3 – 12.3	19.7 – 20.7
0	10.2 – 11.2	18.0 – 19.0
1	9.3 – 10.3	16.1 – 17.1
2	8.5 – 9.5	14.7 – 15.7
3	7.6 – 8.6	13.1 – 14.1
4	6.7 – 7.7	11.7 – 12.7
5	5.7 – 6.7	8.8 – 9.8

Average for special lengths may be decided upon mutually between the manufacturer of the Hard Gelatin Capsule Shells and the user.

Table 3- AverageWall Thickness		
Size	Cap (mm)	Body (mm)
000	0.095 - 0.125	0.095 - 0.125
00	0.095 - 0.125	0.090 - 0.120
0	0.095 - 0.125	0.090 - 0.120
1	0.090 - 0.120	0.087 - 0.117
2	0.090 - 0.120	0.087 - 0.117
3	0.085 - 0.115	0.082 - 0.112
4	0.082 - 0.112	0.082 - 0.112
5	0.082 - 0.112	0.082 - 0.112

Note: Multiply above values by 2 to arrive at norms for double wall thickness

5.8.2 Dimensions of Hard Cellulose Capsule Shells

Hard Cellulose Capsule Shells normally used for the incorporation of medicaments are cylindrical in shape but other shapes are also formed for special requirements. The shells of the capsules consist of two prefabricated cylindrical sections, one end of which is rounded and the other is open. The shells are of various sizes, usually designated by different numbers, 5 being the smallest and 000 the largest. The dimensions of hard cellulose capsule shells tend to vary with the content of moisture in them and the conditions under which they are stored or to which they are exposed. The chemical composition of the shells also influences the extent to which exposure to heat and moisture

affects the dimensions. Nevertheless, the average conventional dimensions (outside diameter, length and wall thickness – single / double) of the capsule shells of sizes 000 to 5 are provided in the table 1, 2 & 3 for the guidance of users. It should be noted that any measurement of reasonable accuracy can be made only under controlled conditions of temperature and humidity. A temperature between 23°and 27°and a relative humidity between 45 per cent and 55 per cent are recommended.

Table 1- Average Outside Diameter		
Size	**Cap (mm)**	**Body (mm)**
000	9.91 – 10.03	9.56 – 9.68
00	8.49 – 8.61	8.15 – 8.27
0	7.60 – 7.72	7.26 – 7.38
1	6.87 – 6.99	6.55 – 6.67
2	6.31– 6.43	6.02 – 6.14
3	5.79 – 5.91	5.51 – 5.63
4	5.28 – 5.39	5.00 – 5.12
5	4.85 – 4.97	4.59 – 4.71

Table 2- Average Length		
Size	**Cap (mm)**	**Body (mm)**
000	12.5 – 13.5	21.7 – 22.7
00	11.3 – 12.3	19.7 – 20.7
0	10.2 – 11.2	18.0 – 19.0
1	9.3 – 10.3	16.1 – 17.1
2	8.5 – 9.5	14.7 – 15.7
3	7.6 – 8.6	13.1 – 14.1
4	6.7 – 7.7	11.7 – 12.7
5	5.7 – 6.7	8.8 – 9.8

Average for special lengths may be decided upon mutually between the manufacturer of the Hard Cellulose Capsule Shells and the user.

Table 3- AverageWall Thickness		
Size	Cap (mm)	Body (mm)
000	0.095 - 0.125	0.095 - 0.125
00	0.095 - 0.125	0.095 - 0.125
0	0.095 - 0.125	0.095 - 0.125
1	0.090 - 0.120	0.090 - 0.120
2	0.090 - 0.120	0.090 - 0.120
3	0.085 - 0.115	0.085 - 0.115
4	0.082 - 0.112	0.082 - 0.112
5	0.082 - 0.112	0.082 - 0.112

Note: Multiply above values by 2 to arrive at norms for double wall thickness

BambuterolHydrochloride.Page 1134

Assay, line4.

Change**from**: Read the volume added between the two points of inflection. Carry out the blank titration.

To: Read the volume added between the two points of inflection.

Cyclosporine.Page. 1487

Para 2

Change **from:** Cyclosporine contains not less than 98.5 per cent and not more than 101.5 per cent of cyclosporine A, $C_{62}H_{111}N_{11}O_{12}$, calculated on the dried basis.

to: Cyclosporine contains not less than 97.0 per cent and not more than 101.5 per cent of cyclosporine A, $C_{62}H_{111}N_{11}O_{12}$, calculated on the dried basis.

Ergotamine Injection. Page no 1677

Para 2, lines3 to 5.

Change **from : ....**not more than 110.0 per cent of the stated amount of ergotamine tartrate, of which 50 to 70 per cent is present as ergotamine tartrate.

to : ....not more than 110.0 per cent of the stated amount of ergotamine tartrate.

Ethanolamine.Page 1701

Related substances. After chromatographic system.Para 2.

Change **to**: Inject 1 µl of the reference solution and the test solution.In the chromatogram obtained with the test solution calculate the content of diethanolamine and triethanolamine using the ratios of the peaks and by reference to the corresponding peaks in the chromatogram obtained with the reference solution. The content of diethanolamineand triethanolamine is not more than 1.0 per cent individually.

Calculate the content of other impurities using the ratios of the peaks and by reference to the peak due to ethanolamine. The content of any other impurity is not more than 0.5 per cent and the sum of the contents of all the impurities is not more than 2.0 per cent.

Clobazam Tablets.Page 4171

Assay.

Change **to:**

Assay. Determine by liquid chromatography (2.4.14) as described underRelated substances with the following modifications.

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 20 mg of Clobazam in 80 ml of mobile phase, mix with the aid of ultrasound, dilute to 100.0 with mobile phaseand centrifuge. Dilute 1.0 ml of the supernatant liquid to 10.0 ml with mobile phase.

Reference solution (a).A 0.002 per cent w/v solution of *clobazam RS* in mobile phase.

Reference solution (b). A 0.01 per cent w/v solution of *7-chloro-1,5-dihydro-5-phenyl-1,5- benzodiazepine-2,4(3H)-dione RS* (*clobazam impurity A RS*) in mobile phase. Dilute 1.0 ml of this solution to 2.0 ml with a 0.1 per cent w/v solution of *clobazam RS* in the mobile phase.

Inject reference solution (b). The test is not valid unless, the resolutionbetween clobazam impurity A and clobazam is not less than 3.0.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{16}H_{13}ClN_2O_2$ in the tablets.

Methotrexate.Page 2191, 4219

Enantiomeric purity.*Reference solution (b).*

Change **to**: Dissolve 4. 0 mg of *methotrexate for system suitability RS* (containing impurity F) in the mobile phase and dilute to 20.0 ml with the mobile phase.

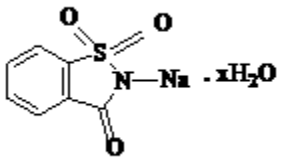
After chromatographic system. Add the following,
The relative retention time with reference to methotrexate (retention time is about 4 minutes) for impurity F is about 1.6.

Phenylephrine Hydrochloride.Page 2478

Phenones.
Delete the test.

Saccharin Sodium.Page 2696

Chemical Structure.
Change **to**:



Molecular Formula.
Change **to**:$C_7H_4NNaO_3S.\ xH_2O$

Sodium Acetate.Page 2733

Aluminum. Lines 6 and 7
Change **from**: ..a mixture of 0.4 ml of *aluminium standard solution (2 ppm Al)*
to: .. a mixture of 2.0 ml of *aluminium standard solution (2 ppm Al)*

Lactic Acid.Page 2049

Methanol and methyl esters. Line 14
Change **from**: 100 g of *methanol*.
to: 100 µg of *methanol*.