Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Halothane

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This draft proposal contains general chapter text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to revisions before publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to arnd-ipc@gov.in , with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	**Details**
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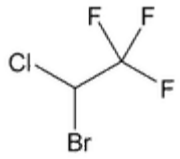
Draft revision published on IPC website for public comments	
Further follow-up action as required.	

Halothane



$C_2HBrClF_3$ Mol. Wt. 197.4

Halothane is ethane, 2-bromo-2-chloro-1,1,1-trifluoro-, (±).

Halothane contains not less than 0.008 per cent and not more than 0.012 per cent of thymol, $C_{10}H_{14}O$ by weight, as a stabilizer.

Category. General anesthetics.

Description. A clear, colorless, mobile, non-flammable, liquid.

Identification

A. Dissolve 1 ml of substances under examination in 25 ml of *carbon disulphide*, determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *halothane IPRS* or with the reference spectrum of halothane. [*NOTE- Use 0.1 mm cells*]

Tests

Acidity or alkalinity. To 20 ml, add 20 ml of *carbon dioxide-free water*, shake for 3 minutes and allow to stand. Separate the aqueous layer and add 0.2 ml of *bromocresol purple solution*. Not more than 0.1 ml of *0.01 M sodium hydroxide* or 0.6 ml of *0.01 M hydrochloric acid* is required to change the colour of the indicator.

Chloride and Bromide. To 25 ml add 25 ml of *water* shake for 5 minutes, and allow the liquids to separate completely. Draw off the water layer, and to 10 ml add one drop of *nitric acid* and 5 drops of *silver nitrate solution*; no opalescence is produced.

Distillation range (2.4.8). Not less than 95.0 per cent distils within a 1° range between 49° and 51°, and not less than 100.0 per cent between 49° and 51°, a correction factor of 0.040° per mm being applied as necessary.

Limit of Nonvolatile Residue. Not more than 1 mg. Evaporate 50 ml of Halothane to dryness in a tared porcelain dish on a steam-bath and dry at 105° for 2 hours.

Refractive Index (2.4.27). 1.369 to 1.371 at 20°.

Relative Density (2.4.29). 1.872 to 1.877 at 20°.

Related substances. Determine by gas chromatography (2.4.13).

Test solution. The substance under examination.

Reference solution. Add 1.0 µl of 1,1,2-trichloro-1,2,2-trifluoroethane (trichlorotrifluoroethane) to 20.0 ml of Halothane.

Chromatographic system
- -a stainless steel column 3.0 m x 2 mm, packed with acid / base washed siliceous each coated with 20 per cent w/w of diisodecyl phthalate,
- -temperature:
  column 60°,
- -injection port and detector at 200°,
- -flame ionization detector,
- -flow rate: 15 ml per minute, using nitrogen as the carrier gas,
- -injection volume: 2µl.

Inject the reference solution. The retention times for 1,1,2-trichloro-1,2,2-trifluoroethane and halothane are 5 and 13 minutes, respectively.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the sum of areas of all the peaks other that halothane does not exceed that due to the added 1,1,2-trichloro-1,2,2-trifluoroethane in the reference solution (0.005 per cent).

Water (2.3.43). Not more than 0.03 per cent, determined on 1.0 g.

Thymol content

Buffer solution. *Alkaline borate buffer pH 8.0.*

Chlorimide solution: A 0.4 per cent w/v solution of *2,6-dibromoquinone-chlorimide* in *ethanol (Note—Prepare a fresh solution for each assay).*

Test solution. Transfer 2 ml of substance under examination to a 100-ml volumetric flask containing 5 ml of *0.25 M sodium hydroxide*, and mix by gentle swirling. Evaporate the substance under a stream of nitrogen, and add 10 ml of the buffer solution and 1 ml of chlorimide solution. Swirl gently, and allow to stand for 15 minutes, accurately timed. Add 3 ml of *0.25 M sodium hydroxide*, and dilute to volume with *water*.

Reference solution (a). A 0.01 per cent w/v solution of *thymol IPRS* in *0.25 M sodium hydroxide*.

Reference solution (b). Pipette 1.0 ml of reference solution (a) into a 100-ml volumetric flask, and add *0.25 M sodium hydroxide* to make the final volume 5 ml. Add 10 ml of buffer solution, mix by gentle swirling, and add 1 ml of chlorimide solution. Allow to stand for 15 minutes, accurately timed. Add 3 ml of *0.25 M sodium hydroxide*, and dilute to volume with *water*.

Reference solution (c). Pipette 3.0 ml of reference solution (a) into a 100-ml volumetric flask, and add *0.25 M sodium hydroxide* to make the final volume 5 ml. Add 10 ml of the buffer solution, mix by gentle swirling, and add 1 ml of chlorimide solution. Allow to stand for 15 minutes, accurately timed. Add 3 ml of *0.25 M sodium hydroxide*, and dilute to volume with *water*.

Reference solution (d). Pipette 5.0 ml of reference solution (a) into a 100-ml volumetric flask, and add *0.25 M sodium hydroxide* to make the final volume 5 ml. Add 10 ml of the buffer solution, mix by gentle swirling, and add 1 ml of chlorimide solution. Allow to stand for 15 minutes, accurately timed. Add 3 ml of *0.25 M sodium hydroxide*, and dilute to volume with *water*.

Blank solution. Pipette 5.0 ml of *0.25 M sodium hydroxide* into a 100-ml volumetric flask. Add 10 ml of the buffer solution, mix by gentle swirling, and add 1 ml of chlorimide solution. Allow to stand for 15 minutes, accurately timed. Add 3 ml of *0.25 M sodium hydroxide*, and dilute to volume with *water*.

Measure the absorbances of reference solution (b), (c), (d), the test solution and blank solution at the maximum at about 590 nm (2.4.7). Plot the readings, and draw the curve of best fit. Read the absorbance of the test solution, and by reference-to-reference solution (a) curve, calculate the percentage of thymol in the weight of Halothane taken.

Storage. Store protected from moisture, preferably of Type NP glass and avoid exposure to excessive heat. Disperse it only in the original container.