European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Certification of Substances Department

Certificate of suitability
No. R1-CEP 2006-227 - Rev 02

Name of the substance:
FORMOTEROL FUMARATE DIHYDRATE

Name of holder:
VAMSI LABS LIMITED
A-14, A-15, A-31, A-32 and A-33, M.I.D.C. Area
Chincholi
India-413 255 Solapur, Maharashtra

Site(s) of production:
SEE ANNEX 1

THIS CERTIFICATE SUPERSEDES THE PREVIOUS CERTIFICATE
R1-CEP 2006-227 - REV 01

After examination of the information provided on the manufacturing method and subsequent processes (including purification) for this substance on the site(s) of production listed in annex, we certify that the quality of the substance is suitably controlled by the current version of the monograph **FORMOTEROL FUMARATE DIHYDRATE** no. 1724 of the European Pharmacopoeia, current edition including supplements, only if it is supplemented by the test(s) mentioned below, based on the analytical procedure(s) given in annex.

– Test for residual solvents by gas chromatography (Annex 2)

Methanol	not more than 3000 ppm
2-Propanol	not more than 5000 ppm

In the last steps of the synthesis water is used as solvent.

The re-test period of the substance is 5 years if stored in double polyethylene bags (outer black) placed in a polyethylene drum.

The holder of the certificate has declared the absence of use of material of human or animal origin in the manufacture of the substance.

The submitted dossier must be updated after any significant change that may alter the quality, safety or efficacy of the substance.

Address: 7 Allée Kastner, CS 30026
F-67081 Strasbourg (France)
Tel: +33 (0) 3 88 41 30 30 – e-mail: cep@edqm.eu
Internet: https://www.edqm.eu

Manufacture of the substance shall take place in accordance with the Good Manufacturing Practice and in accordance with the dossier submitted.

Failure to comply with these provisions will render this certificate void.

This certificate is renewed from **19 June 2014** according to the provisions of Resolution AP-CSP (07) 1, and of Directive 2001/83/EC and Directive 2001/82/EC and any subsequent amendment, and the related guidelines.

This certificate has two annexes, the first of 1 page and the second of 2 pages.
This certificate has:
lines.

On behalf of the
Director of EDQM

Strasbourg, 28 July 2022

DECLARATION OF ACCESS *(to be filled in by the certificate holder under their own responsibility)*

Vamsi Labs Limited, as holder of the certificate of suitability

R1-CEP 2006-227 - Rev 02 for Formoterol fumarate dihydrate

hereby authorises .....
(*name of the pharmaceutical company*)

to use the above-mentioned certificate of suitability in support of their application(s) for the following Marketing Authorisation(s): (*name of product(s) and marketing number(s), if known*)

The holder also certifies that no significant changes to the operations as described in the CEP dossier have been made since the granting of this version of the certificate.

Date and Signature (*of the CEP holder*):

European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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Annex 1: Site(s) of production for R1-CEP 2006-227 - Rev 02

Production of Formoterol fumarate dihydrate:

VAMSI LABS LIMITED
A-14, A-15, A-31, A-32 and A-33, M.I.D.C. Area
Chincholi
India-413 255 Solapur, Maharashtra

Additional In-house test		
09.	Residual Solvents (GC-Headspace)*	
	Chromatographic conditions for GC	Column: DB-624, (6% Cynopropylphenyl and 94 % Dimethylpolysiloxane) 30 m x 0.53 mm ID, 3.00 µm or Equivalent. Name of detector:FID (Flame-ionization detector) Injection system:Auto Carrier gas :Nitrogen for chromatography. Instrument Parameters Initial oven temperature: 35°C Initial time:10 min. Rate:15°C/min. Final Oven temperature:240°C Final time :2 min. Injector temperature :225°C Split ratio:10:1 FID temperature (1):250°C Carrier gas (N2) flow:3.0 ml/min Spilt flow:27 ml/min.

QUALITY ASS. VAMSI LABS SOLAPUR

Prepared By	Checked By	Approved By
Date & Sign Vilay 16/05/14	Date & Sign 20/05/2014	Date & Sign 20/05/14
QA Officer	QA-Executive	Head-QA/RA

Sr. No.	Tests	Standard Testing Procedure
	Chromatographic conditions for Headspace	Head Space Parameters Vial oven temperature:80°C Needle temperature :90°C Injection time :0.1 min. With drawl time:0.2 min. Pressurizing time :0.2 min. Thermo stating time:20 min. Head space pressure:15 psi Vial vent :Off GC Cycle time:35 min.
	Diluent	DMSO Note: Purity of diluent used in the analysis should be checked for any Impurities eluting at the same RT as that of the different residual solvents analyzed by this method.
	Preparation of blank solution:	Transfer 5 ml of diluent to a headspace vial and seal the vial immediately.
	Preparation of standard solution:	Accurately weigh about 0.6000 g Methanol, 1.0000 g Ethanol, 1.0000 g of Acetone, 1.0000 g of Ethyl acetate and 1.0000 g of Isopropyl alcohol, 0.1780 g of Toluene, and 0.0580 g of n-hexane in 100 ml volumetric Flask containing about 10 ml of diluent. Make up the volume with diluent. Further, dilute 10 ml of this solution to 100 ml of diluents. Transfer 5 ml of diluent to a headspace vial and seal the vial immediately.
	Preparation of sample solution:	Accurately weigh and transfer about 1.0000 g of sample to the headspace vial adds 5.0 ml of diluent and seal the vial immediately.
	Evaluation of blank solution	Place the sealed vial of the blank solution in the magazine and run the headspace. No peak should be observed at the retention time of analyte.
	System Suitability	Inject the standard solution in to the chromatograph using above chromatographic parameters and note the peak areas of eluting Peaks from the chromatographic report. The system is suitable for analysis, if and only if; The relative standard deviation of area of six replicate injections for all solvents is not more than 15.0% & the resolution between two adjacent components is not less than 1.5.
	Injection sequence system suitability	S. No. / Sample information / No. of injections 1. Diluent Blank 01 2. Standard solution 06 3. Sample solution 01

* Validated in-house test procedure.

Prepared By	Checked By	Approved By
Date & Sign 16/05/14	Date & Sign 20/05/2014	Date & Sign 26/05/14
QA Officer	QA-Executive	Head-QA/RA