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. R0-CEP 2020-172 - Rev 01

Name of the substance:
CLENBUTEROL HYDROCHLORIDE

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
R0-CEP 2020-172 - REV 00

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 **CLENBUTEROL HYDROCHLORIDE** no. 1409 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.

Any unspecified impurity detected by the test for related substances of the monograph is limited to not more than 0.10%.

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

Methanol	not more than 3000 ppm
Isopropyl alcohol	not more than 5000 ppm

The following elemental impurity classified in ICH Q3D is intentionally introduced in the manufacture of the substance: Selenium.

The re-test period of the substance is 60 months if stored in polyethylene bags (outer black), placed in a polyethylene container.

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

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

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 granted within the framework of the procedure established by the European Pharmacopoeia Commission [Resolution AP-CSP (07) 1] for a period of five years starting from **30 March 2022**. Moreover, it is granted according to the provisions 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 4 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

R0-CEP 2020-172 - Rev 01 for Clenbuterol hydrochloride

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*):

Certification of Substances Department

Annex 1: Site(s) of production for R0-CEP 2020-172 - Rev 01

Production of Clenbuterol hydrochloride:

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

Residual solvent by GC:	In-house
Reagents and chemicals: Methanol : AR grade or equivalent Ethanol : AR grade or equivalent Isopropyl alcohol : AR grade or equivalent Ethyl acetate : AR grade or equivalent 1,4 Dioxane : AR grade or equivalent Benzene : AR grade or equivalent	
Chromatographic conditions: 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.	

Standard testing procedure			Reference No.
Instrument Parameters:			
Initial oven temperature	:	50°C	
Hold time	:	10 min.	
Rate	:	15°C/min.	
Final Oven temperature	:	250°C	
Final time	:	2 min.	
Injector temperature	:	250°C	
FID temperature (1)	:	250°C	
Carrier gas (N2) flow	:	3.0 ml/min	
Split ratio	:	5:1	
Head Space Parameters			
Vial oven temperature	:	80°C	
Loop temperature	:	90°C	
Transfer line temperature	:	100°C	
Injection time	:	0.1 min.	
Loop Fill time	:	0.2 min.	
Loop Equilibration time	:	0.05 min	
Vial Pressurization time	:	0.2 min.	
Vial Equilibration time	:	12 min.	
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.			

Standard testing procedure	Reference No.
Preparation of standard stock solution: Accurately weigh about 0.60 g of methanol, 1.0 g of ethanol, 1.0 g Isopropyl alcohol, 1.0 g of Ethyl Acetate and 0.076 g of 1,4 Dioxane in 100 ml volumetric flask containing about 10 ml of diluent. Make up the volume with diluent.	
Preparation of standard Benzene stock solution: Accurately weigh about 0.050 gm of benzene in 25 ml DMSO and further take 1 ml and dilute to 100 ml with diluent.	
Preparation of standard solution: Take accurately 10 ml of standard stock solution and 2 ml of benzene stock solution and dilute to 100 ml with diluent.	
Preparation of sample solution: Accurately weigh and transfer about 1.0 g of sample to the headspace vial and add 5.0 ml of diluent and seal the vial immediately.	Sample quantity 1.0 gm
Preparation of Blank: Transfer 5 ml of diluent into a dried vial 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% and Resolution between two peaks is not more than 1.5	

Standard testing procedure	Reference No.

Injection sequence:

Sr. No.	Name of Injection	No. of Injection
01.	Blank	01
02.	Standard Solution	06
03.	Sample solution	01

Calculation

Calculated the content of each residual solvent (in ppm) by using the following formula:

$$= \frac{r_U}{r_S} \times \frac{C_S}{C_U} \times 1000000$$

r_U: Peak response of each solvent from the sample solution.

r_S: Peak response of each solvent from the standard solution.

C_S: Concentration of standard solution.

C_U: Concentration of sample solution.