European Directorate for the Quality of Medicines & HealthCare

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

Certification of Substances Division

Certificate of suitability No. R0-CEP 2008-167-Rev 00

Name of the substance:
NALTREXONE HYDROCHLORIDE

Name of holder:
RUSAN PHARMA LTD.
58-D, Government Industrial Estate
Charkop, Kandivli (West)
India-400 067 Mumbai

Site(s) of production:
RUSAN PHARMA LTD.
Plot No 6406, G.I.D.C.
Near Hoechst Chokadi, Dist. Bharuch
India-393 002 Ankleshwar, Gujarat

After examination of the information provided on the manufacturing method and subsequent processes (including purification) for this substance on the site(s) of production mentioned above, we certify that the quality of the substance is suitably controlled by the current version of the monograph **NALTREXONE HYDROCHLORIDE** no. 1790 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 other impurity than those mentioned in the monograph and detected by the test for related substances of the monograph is individually limited to not more than 0.10%.

– Test for residual solvents by gas chromatography (Annex 1)
Dichloromethane not more than 600 ppm

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

The test for Ethanol described in the monograph is not necessary since this solvent is not used in the synthesis.

The re-test period of the substance is 24 months if stored in LDPE / Aluminium / PET bags placed in a polythene bag.

Address: 7, allée Kastner, CS 30026 - F - 67081 Strasbourg (France)
Telephone: 33 (0) 3 88 41 30 30 - Fax: 33 (0) 3 88 41 27 71 - e-mail: cep@edqm.eu
Internet : http://www.edqm.eu

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.

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 (93) 5 as amended] for a period of five years starting from **7 January 2010**. 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 one annex of 2 pages.
This certificate has:
lines.

On behalf of the
Director of EDQM

Strasbourg, 7 January 2010

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

Rusan Pharma Ltd., as holder of the certificate of suitability

R0-CEP 2008-167-Rev 00 for NALTREXONE 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)*:

Address: 7, allée Kastner, CS 30026 - F - 67081 Strasbourg (France)
Telephone: 33 (0) 3 88 41 30 30 - Fax: 33 (0) 3 88 41 27 71 - e-mail: cep@edqm.eu
Internet : http://www.edqm.eu

12) Residual solvent : In-house Gas Chromatography

Acetone and Dichloromethane in Naltrexone Hydrochloride

Chromatographic system

Column:	10 % OV – 210; 2M,Dia 0.31cm, mesh 80/100
Column Temperature:	Initial 50 deg C 50°C for 2 minutes 100°C at 5deg C 100°C for 5 minutes
Injector Temperature:	210°C
Detector Temperature (FID):	230°C
Flow of carrier gas (Nitrogen):	30 ml / min

Std Preparation:

Transfer about 150 mg of acetone and 90 mg of Dichloromethane accurately weighed, to a 100 ml volumetric flask containing 80 ml Dimethylformamide, shake, dilute to 100 ml with Dimethylformamide (I). Dilute 2.0 ml of (I) to 10ml with Dimethylformamide (II)

Sample Preparation:

Take 3.0 g of sample in centrifuge tube, add 10 ml of Dimethylformamide. Centrifuge it if necessary.

Procedure: Inject 1 microlitre of the sample preparation and std preparation and record the peak responses.

Calculation: Acetone

$$\frac{\text{Sample area}}{\text{Standard area}} \times \frac{\text{Wt. of std. in mg}}{100} \times \frac{2.0}{10} \times \frac{10}{\text{Wt. of spl in mg}} \times 1000000$$

= Acetone content in ppm

Calculation: Dichloromethane

$$\frac{\text{Sample area}}{\text{Standard area}} \times \frac{\text{Wt. of std in mg}}{100} \times \frac{2.0}{10} \times \frac{10}{\text{Wt. of spl in mg}} \times 1000000$$

= Dichloromethane content in ppm