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Location: Moldova

CERTIFICATE OF A DIAGNOSTIC PRODUCT

089693

No. of Certificate: MFG/COPP/ARKRAY/2018/

Exporting (Certifying) Country: **INDIA**
Importing (requesting) Country: **IRAN**

1. Name and dosage form of products: Tuberculin Diluted: Tuberculin P.P.D. 2 TU/0.1 ml for Mantoux Test Only

1.1 Active ingredient (s) and amount (s) per unit dose :
Active Ingredient : Tuberculin PPD
Amount per unit : 2 Tuberculin units per 0.1 ML dose
Complete qualitative composition including excipients, N.A.

1.2 Is this product licensed to be placed on the market for use in the exporting country? Yes ☒ No ☐

1.3 Is this product actually on the market in the exporting country ? Yes ☒ No ☐

If the answer to 1.2 is yes., continue with section 2 A and If the answer to 1.2 is no. continue section 2 B

2A.1 Number of product license : **Manufacturing Lic. No. G/28/1507 Dtd. 26.02.2015.**	2B.1 Applicant for certificate (name and address) **N.A.**
2A.2 Product license holder : M/s. **ARKRAY HEALTHCARE PVT. LTD.** Plot No. 336, 338, 340, Road No. 3 G.I.D.C. Sachin Dist.: Surat - 394230 **Gujarat State, INDIA**	2B. 2 Status of applicant : **N.A.** a ☐ b ☐ c ☐ d ☐ 2B.2.1 For categories b and c the name and address of the manufacturer producing the dosage form :
2A.3 Status of product – license Holder : Manufacturer of the dosage form a ☒ b ☐ c ☐	2B.3 Why is marketing authorization lacking? **N.A.** Not Required ☒ Not Requested ☐ Under Consideration ☐ Refused ☐
2A. 4 Is summary basis of Approval appended? N.A. Yes ☐ No ☐ **Formulation is based on Indian Pharmacopoeia Volume II Pg. No. 785-786**	2B. 4 Remarks : **N.A.**
2A.5 Is the attached officially approved product information complete and consonant with the license ? Yes ☒ No ☐ Not Provided ☐	
2A. 6 Applicant for certificate if different from license holder **: Licence Holder is same as Applicant**	

COMMISSIONER, FOOD & DRUGS CONTROL ADMINISTRATION GUJARAT STATE GANDHINAGAR

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced?
Yes ☒ No ☐ Not applicable ☐
If no or not applicable proceed to question 4
3.1 Periodically of routine inspections (Years) : **Annually (Once in a year)**
3.2 Has the manufacture of this type of dosage form been inspected? Yes ☒ No ☐

4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product?
Yes ☒ No ☐ Not applicable ☐

If no, explain:

This Certificate valid up to **2 Years from Date of Issue**

Address of certifying authority :

The Commissioner Food & Drug Control Administration
1st Floor, Block No. 8, Dr. Jivraj Mehta Bhavan,
Gandhinagar, Gujarat State, INDIA
Tel: 91-79-232 53417 Fax: 91-79-232 53400
Date of Approval:

Name of the Authorized Person : **Mr. V. R. SHAH**

Signature:
Stamp and date:
Joint Commissioner
Food & Drugs Controls Administration
Gujarat State
1 AUG 2018

Food & Drugs Control Administration

BLOCK NO. 8, 1St FLOOR, Dr. JIVRAJ MEHTA BHAVAN,
GANDHINAGAR, GUJARAT STATE, INDIA. PIN : 382010

Certificate No. : **S-GMP/1705122**

G.M.P. CERTIFICATE

This is to certify that M/s. **ARKRAY HEALTHCARE PVT. LTD., PLOT NO 336,338, 340, ROAD NO 3, G.I.D.C, SACHIN -394 230, Dist -SURAT** *is holding valid drug manufacturing licenses in Form No.* **25 & 28** *bearing No.* **G/25/2083 & G/28/1507** *respectively issued by this administration under the provisions of Drugs & Cosmetics Act 1940 & Rules there under. Under the said licenses the firm is permitted to manufacture & sell drugs covered under the following categories.*

Dosage Form (s)	*Category (ies)*
Diagnostic Reagents & Kits	**General**

The firm has employed competent technical staff to undertake manufacturing & testing of the permitted drugs. They are following **GOOD MANUFACTURING PRACTICES** *in manufacturing and testing as laid down under the* **REVISED SCHEDULE-M** *of Drugs & Cosmetics Act 1940 & Rules There under.*

The manufacturing plant is subjected to inspection at suitable intervals by competent authority.

This certificate is valid from Dt : **31/05/2017** *to* **30/05/2019.**

COMMISSIONER, FOOD & DRUGS CONTROL ADMINISTRATION * GANDHINAGAR * GUJARAT STATE

(Dr. H. G. KOSHIA)
Commissioner
Food & Drugs Control Administration
Gandhinagar, Gujarat State

Email : *comfdca@gujarat.gov.in*

Phone : *91-79-23253417, Fax : 91-79-232-53400*

arkray

List of Products covered under Schedule C and C1, excluding Schedule X to be manufactured by M/s. ARKRAY Healthcare Pvt. Ltd., Plot No. 336, 338, 340, Road No. 3, G.I.D.C., Sachin - 394 230. Dist. Surat, India, under the Drugs Manufacturing Licence No. G/28/ in Form No. 28.

arkray healthcare pvt. ltd.
(Comprises of former IVD Business Undertaking of Span Diagnostics Ltd.)
Factory :
Plot no. 336, 338, 340, Road no. 3,
G.I.D.C.,Sachin - 394230, (Surat), India.
telephone: +91-261-239 7712
fascimile : +91-261-239 7719
URL : http://www.arkray.co.in

LIST OF DIAGNOSTIC REAGENTS & KITS

112 APTT-EA-An Ellagic Acid Activated Reagent for Partial Thromboplastin

This kit includes:
Reagent No. 1: APTT-EA (Ready to use)
Reagent No. 2: Sodium Citrate 3.2 gm%
Reagent No. 3: Calcium Chloride 0.02 M

113 Tuberculin Diluted: Tuberculin P.P.D. IP 10 TU / 0.1 mL for Mantoux Test only

114 Tuberculin Diluted: Tuberculin P.P.D. IP 5 TU / 0.1 mL for Mantoux Test only

115 Tuberculin Diluted: Tuberculin P.P.D. IP 2 TU / 0.1 mL for Mantoux Test only

116 Tuberculin Diluted: Tuberculin P.P.D. IP 1 TU / 0.1 mL for Mantoux Test only

117 Tuberculin Diluted: Tuberculin P.P.D. 10 TU / 0.1 mL for Mantoux Test only (For Export Only)

118 Tuberculin Diluted: Tuberculin P.P.D. 5 TU / 0.1 mL for Mantoux Test only (For Export Only)

119 Tuberculin Diluted: Tuberculin P.P.D. 2 TU / 0.1 mL for Mantoux Test only (For Export Only)

120 Tuberculin Diluted: Tuberculin P.P.D. 1 TU / 0.1 mL for Mantoux Test only (For Export Only)

121 Lyophilized Tuberculin PPD I.P. – For Tender Only 1 TU / 0.1 mL, For Mantoux Test Only

122 Lyophilized Tuberculin PPD I.P. – For Tender Only 2 TU / 0.1 mL, For Mantoux Test Only

123 Lyophilized Tuberculin PPD I.P. – For Tender Only 5 TU / 0.1 mL, For Mantoux Test Only

124 Lyophilized Tuberculin PPD I.P. – For Tender Only 10 TU / 0.1 mL, For Mantoux Test Only

125 TB Test Kit – 5 TU / 0.1 mL: For Export Only

COMMISSIONER, FOOD & DRUGS CONTROL ADMINISTRATION GANDHINAGAR GUJARAT STATE

For, Commissioner
Food & Drugs Control Administration
Gujarat State

26 FEB 2015 to 25 FEB 2020

COMMISSIONER of, 1907K
Food & Drugs Control Administration,
Block No.8, 1st floor, Dr. Jivraj Mehta Bhavan,
GANDHINAGAR.- 382 010
DATE :

27 FEB 2015

To,
ARKRAY HEALTHCARE PVT. LTD.,
PLOT No. 336, 338, 340, ROAD No. - 3, G.I.D.C.,
SACHIN,,
DIST -SURAT.- 394 230

SUB : Grant of **FRESH LICENCE**

Sir,

REF : Your application in form No. **24 & 27**, both Dated : **09/02/2015**

Licences having following details has been granted with revised Schedule " M ".

I. Details of Licence :

Form No.	Licence No.	Validity		Category
		From	To	
25	G/25/2083	26/02/2015	25/02/2020	DIAGNOSTIC REAGENTS & KITS
28	G/28/1507	26/02/2015	25/02/2020	DIAGNOSTIC REAGENTS & KITS

II. Approved Technical Person (Manufacturing Section)

1 AS PER LIST APPROVED AND ANNEXED

Approved Technical Person (Testing Section)

1 AS PER LIST APPROVED AND ANNEXED

Further you are also permitted to get your raw materials and finished products tested at any govt. approved public testing laboratories holding approval in form 37 under Drugs & Cosmetics Rules 1945. only for those tests which require sophisticated equipments.

Yours faithfully,

for Commissioner,
Food & Drugs Control Administration.

Encl:- 1. Original Licences
2. List of Products Approved
3. Draft Labels

NO.MFG/ARKRAY/ /B Dt.

Copy with a copy of approved list of products forwarded to :-

1) The Assistant Commissioner, **SURAT.**
2) The Statistical Cell, (G-Branch)

for Commissioner,
Food & Drugs Control Administration.

FRESH LICENCE

FORM 25

(See Rule 70)

Licence to manufacture for sale (or for distribution) of drugs other than those specified in Schedule C, C(1) and X

Number of licence and date of issue G/25/2083 Date- 26/02/2015

1. DIRECTORS of M/s. ARKRAY HEALTHCARE PVT. LTD. is hereby licensed to manufacture the following categories of drugs being drugs other than those specified in Scheduled C, C(1), and X to the Drugs & Cosmetics Rules, 1945, on the premises situated at PLOT No. 336, 338, 340, ROAD No. - 3, G.I.D.C., SACHIN, DIST -SURAT - 394 230.

under the direction and supervision of the following (competent technical staff):-

(a) Competent technical staff (Names)	As Per List Approved & Annexed
(b) Names of Drugs (each item to be separately specified)	As Per List Approved & Annexed

2. The licence authorizes the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence, subject to the conditions applicable to licence for sale.

3. The licence shall be in force From: 26/02/2015 To 25/02/2020

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Signature :

Designation : Commissioner
Food & Drugs Control Administration
Gujarat State.

Date:- 27/02/2015

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.
2. Any change in the (competent technical staff) named in the licence shall be forthwith reported to the Licensing Authority.
3. If the licensee wants to manufacture for sale additional items of drugs not included above he should apply to the Licensing Authority for the necessary endorsement as provided in Rule 69(5). This licence will be deemed to extend to the categories so endorsed.
4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

FDCA/GUJARAT/25,28/876

FRESH LICENCE

FORM 28

(See Rule 76)

Licence to manufacture for sale (or for distribution) of drugs specified in Schedule C, C(1) excluding those specified in schedule X

Number of licence and date of issue No. G/28/1507 Dated 26/02/2015

1. **DIRECTORS** of M/s. **ARKRAY HEALTHCARE PVT. LTD.** is hereby granted licence to manufacture at the premises situated at the **PLOT No. 336, 338, 340, ROAD No. - 3, G.I.D.C., SACHIN, DIST -SURAT - 394 230.**

   the following drugs being drugs specified in schedules C & C(1) Excluding those specified in sch. X to the Drugs and Cosmetics Rules 1945.

   Names of Drugs : **As Per List Approved & Annexed**

2. **Names of approved competent technical staff:** **As Per List Approved & Annexed**

3. The licence authorizes the sale by way of wholesale dealing by the licensee and storage for sale by the licencee of the drugs manufactured under the licence, subject to the conditions applicable to licences for sale.

4. The licence will be in force From **26/02/2015** To **25/02/2020**

5. The licence is subject to the conditions stated below and to such other conditions as may be specified in the rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Signature :

Designation : Commissioner
Food & Drugs Control Administration
Gujarat State.

Date- 27/02/2015

COMMISSIONER FOOD & DRUGS CONTROL ADMINISTRATION GANDHINAGAR GUJARAT STATE

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.
2. If the licensee wishes to undertake during the currency of the licence the manufacture of any drug specified in Schedule C and C(1) (excluding those specified in Schedule X) not included above, he should apply to the Licensing Authority for the necessary endorsement as provided in Rule 75(3). This licence will be deemed to extend to the items so endorsed.
3. Any change in the (competent technical staff) shall be forthwith reported to the Licensing Authority.
4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. 0Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed Constitution.)

FDCA/GUJARAT/25,28/876

TUBERCULIN PPD
(DILUTED)
(Code No. 18411)
For Mantoux Test

Diagnostic Reagent for *in vivo* detection of sensitisation by *Mycobacterium tuberculosis.*

The Tuberculin Skin Test (TST) is the most commonty used test to detect exposure to *Mycobacterium tuberculosis,* being used in epidemiological surveys, clinical evaluation of patients with suspected active tuberculosis, and assessment of anti-tuberculous drug therapy. For diagnostic purpose, an intradermal Mantoux Test is performed with different dilutions of Tuberculin PPD. In developed countries, dose of 5 or 10 Tuberculin Units (TU) of PPD is commonly used**[1]**. Whereas, in developing countries, such as India, with high prevalence of Tuberculosis, 1 TU is the recommended dose as per the WHO guidelines **[2]**. International Union against Tuberculosis & Lung Diseases (IUATLD) has also suggested the dose of 2 TU for tuberculin surveys **[3]**. SPAN's Tuberculin PPD (1TU/2TU/5TU/10TU) is a diluted and ready-to-use solution for performing Mantoux test. Source material is calibrated against Batch RT 23 manufactured by Statens Serum Institute, Denmark **[4]**. It is diluted with a special buffer containing Tween-80 as a stabilizer **[5]**.

PRINCIPLE

Infection with *Mycobacterium tuberculosis* results in hypersensitivity to tuberculoprotein. Intradermally injected purified Tuberculin PPD produces erythema and induration of the skin around the point of injection. The diameter of induration is directly proportional to the degree of sensitization.

ADVANTAGES OF SPAN'S TUBERCULIN PPD

1. Accurate interpretations of response, because every batch is carefully standardised by guinea pig assay followed by clinical trials on human volunteers.
2. No risk of non-specific reactions.
3. Supplied in convenient ready-to-use form.
4. No loss of potency due to adsorption on glass wall of Container.
5. Highly economical.

STORAGE & STABILITY OF REAGENT

Tuberculin PPD (diluted) is stable at 2-8^{0} C till the expiry date mentioned on the label of the vial. (Do not freeze). Protect the reagent from light.

PRECAUTIONS

1. Tuberculin PPD has affinity for glass and plastic surfaces. Hence do not transfer PPD solution to other containers and do not hold it in syringes for longer time.
2. A separate sterilized syringe and needle should be used for each individual patient to prevent possible transmission of infectious agents from one person to another.
3. Syringes that have previously been used with histoplasmin, blastomycin or other similar antigens should not be used for PPD.
4. As with any biological product, epinephrine should be immediately available to treat anaphylactoid or acute hypersensitivity reaction, although such reactions are extremely rare with PPD.
5. Avoid subcutaneous injection. After subcutaneous injection local reaction may not develop, but a general febrile reaction and/or exacerbation or inflammation around old tuberculous lesions may occur in highly sensitive individuals.
6. Avoid vigorous shaking of the container.

TEST PROCEDURE

Standard method of Mantoux TEST

Mantoux test is performed by intradermally injecting SPAN'S Tuberculin PPD of desired strength with tuberculin syringe (Luer Lock recommended).

1. The preferred site for the test is the flexor or dorsal surface of the forearm about 4 inches below the elbow joint.
2. Clean the skin at the chosen site with 70% alcohol or spirit and allow to dry.
3. Clean the stopper of the PPD vial with 70% alcohol or spirit and draw 0.1 ml of Tuberculin PPD solution into the sterile tuberculin syringe fitted with a short 26-gauge needle.
4. Inject PPD intradermally by inserting the tip of the needle into the most superficial layers of the skin with needle bevel pointing upwards. As the solution is injected, a pale white bleb, 6 to 10 mm in diameter will rise at the needle point. This will be quickly absorbed and hence no dressing is required.

Note : If the PPD is inadvertently injected subcutaneously, no bleb will from, or if a significant part of the dose leaks from the injection site, the test should be repeated immediately at another site, 5 cms away from the first site.

RESULTS & INTERPRETATION

Result of Mantoux test should be read between 48 to 72 hours after the injection. Induration only should be considered while interpreting the test. The diameter of induration should be measured transversely to the long axis of the forearm and recorded in millimeter.

Erythema of less 10 mm should be disregarded. If the diameter of erythema is greater than 10 mm and induration is absent the injection may have been made too deeply and retesting is Indicated.

REACTIONS ARE CLASSIFIED AS FOLLOWS :

Positive : Induration measuring 10mm or more. This indicates hypersensitivity to tuberculoprotein and indicates past or present infection with *Mycobacterium tuberculosis*

Doubtful : Induration measuring between 5 and 9 mm. Retesting is indicated at another site. This retesting is desirable to rule out cross reactions from other mycobacterial infections.

Negative : Induration of less than 5 mm. This indicates lack of hypersensitivity to tuberculoprotein and tuberculous infection is highly unlikely.

It should be noted that reactivity to tuberculin may be depressed or suppressed for as long as four weeks following viral infections, live-virus vaccines (e.g. measles, smallpox, polio, rubella, mumps, etc.) or by the administration or corticosterioids. Malnutrition may also have a similar effect. When it is of great diagnostic importance, a negative test should be accepted as proof of absence of hypersensitivity only after normal reactivity to non-specific irritants has been demonstrated. Intradermal injection of 0.1 ml % solution of Codeine is recommended for the demonstration of on specific cutaneous reactivity. A positive tuberculin reaction does not necessary signify the presence of active disease. Further diagnostic procedures should be carried out before diagnosis of tuberculosis is made.

WHY FALSE NEGATIVES ?

False negative reactions may be caused by one or more of the following :

1. Subcutaneous injection.
2. Loss of potency due to prolonged exposure to heat or light.
3. Bacterial contamination of PPD solution.

USES

1. Diagnosis or suspected infection by *Mycobacterium tuberculosis* in young children.
2. Epidemological survey to determine the incidence of tuberculosis in a community.
3. To separate positive and negative reactors and to access the response to vaccination by sample testing after mass immunization campaigns.
4. Recognizing tuberculosis in cattle.
5. As a post vaccination check of the efficacy of BCG vaccination.

PRESENTATION :

Strength	Packsize	Code No.
1TU PPD / 0.1 ml	5 ml	18411 B
2TU PPD / 0.1 ml	5 ml	18411 C
5TU PPD / 0.1 ml	5 ml	18411
10TU PPD / 0.1 ml	5 ml	18411 A

REFERENCES :

1. Stuart R.L, A paired comparison of tuberculin skin test results in health care workers using 5 TU and 10 Tu truberculin. *Thorax* (2000), **55,** p 693-695
2. World Health Organization : The WHO standard tuberculin test (1963), *WHO/TB/Tech. Guide/3.*
3. Annadottir Rieder H.L. et.al., Guidelines for conducting skin test surveys in high prevalence countries, *Tubercle* & *Lung Dis.* (1996), **77** (suppl)
4. Magnusson M. et.,al., Preparation of purified tuberculin RT23, *Bull.* WHO (1958), **19**, p 829
5. Magnusson M., Diluents for stabilization of tuberculin. *Bull.* WHO (1958), **19,** p 799

ISO 9001:2000 WHO cGMP

SPAN

Manufactured by :

Span Diagnostics Ltd.

Plot No. 336,338,340,Road No.3, G.I.D.C.,
SACHIN 394 230 (Surat) INDIA.

my trusted partner IN DIAGNOSIS

For Technical Support & Queries Contact
Customer Service Cell (CSC),
Span Diagnostics Ltd.
173-B, New Industrial Estate, Udhna, Surat - 394 210, INDIA.
Phone No.: + 91 261 227 7211 Fax: + 91 261 227 9319

Email: span@spandiag.com **Web : www.span.co.in**

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