MINUTES OF 298TH MEETING OF REGISTRATION BOARD HELD ON 18TH JANUARY, 2021

298th meeting of Registration Board was held on 18th January, 2021 in the Committee Room of Drug Regulatory Authority of Pakistan, G-9/4, Islamabad. The meeting was chaired by Dr. Obaidullah, Director, Pharmaceutical Evaluation & Registration Division, DRAP. The meeting started with recitation of the Holy Verses.

Following members attended the meeting:

1.	Dr. Noor-us-Saba, Director, Biological Evaluation & Research Division, DRAP	Member
2.	Mr.Akhter Abbas Khan, Additional Director (QA&LT), DRAP	Member
3.	Mr. Abdullah, Additional Director (PE&R), DRAP.	Member/ Secretary

Following members attended the meeting via Zoom video link.

1.	Lt. Gen. (R) Dr. Karamat Ahmed Karamat HI-M, SI-M, Former Surgeon General Pakistan	Member
2.	Dr. Rafeeq Alam Khan, Meritorious Professor, Faculty of Pharmacy, Ziauddin University, Karachi	Member
3.	Maj.Gen. (R) Dr. Tahir Mukhtar Sayed, Inspector General (Hospitals), Fauji Foundation, Rawalpindi	Member
4.	Dr. Qurban Ali, Ex-Director General, National Veterinary Laboratories, Islamabad	Member
5.	Mr. Iftikhar A.Choudhary, Hospital Pharmacist, Lahore	Member
6.	Dr. Amanullah Khan, Director, Drugs Testing Laboratory, Quetta. Government of Balochistan	Member
7.	Syed Adnan Rizvi, Director, Drugs Testing Laboratory, Karachi. Government of Sindh	Member
8.	Mr. Zohaib Abbas Khan, Director Technical, DTL Rawalpindi	Member
9.	Ms. Saima Kanwal, Representative of IPO, Islamabad.	Member

Prof. Brig. (R) Dr. Muzammil H. Najmi, Chairman Committee on Evaluation of Clinical Trials also joined the meeting via zoom link.

DRAP Authority in its 101st meeting held on 06-01-2021, while exercising its power under Rule 26 of Drugs (LRA) Rules amended via SRO 713 (I)/ 2018 dated 08-06-2018, allowed to submit registration application on Form-5/ Form 5-A/ Form 5-D instead of Form 5F for registration of COVID-19 vaccines till 06-06-2021.

Director, BE&R assisted by respective Add. Director and Assistant Directors presented the agenda.

Item No. I Division of Biological Evaluation & Research

Priority Approval/ Emergency Use Authorization of COVID-19 Vaccines.

1. M/s National Institute of Health, Islamabad

1.	**Name and address of Importer**	M/s National Institute of Health, Park Road ChakShahzad, Islamabad.
	Detail of DSL	Applied for grant of Drug Sale License to District Health Authorities vide Diary no. 14 dated 18-01-2021
	Name and address of Manufacturer	M/s Beijing Institute of Biological Products Co., Ltd., No. 6 & 9, Boxing 2nd Road, Economic-Technological Development Area, Beijing, 100176, China.
	Brand Name +Dosage Form + Strength	SARS-CoV-2 Vaccine (Vero Cell), Inactivated
	Diary No. Date of R& I & fee	Dy. No. 2028 (R&I) dated 18-01-2021 Rs. 100,000/- Dated 18-01-2021
	Composition	Each Pre-filled Syringe (0.5ml) contains: Inactivated SARS-CoV-2 antigen….6.5U
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	24 months (2^0C-8^0C)
	Document Details	i. Copy of letter on the inclusion of COVID-19 Vaccine for Emergency Use (Trial) dated 23-07-2020 issued by The State Council's Joint Prevention and Control Mechanism for the COVID-19 Pandemic. ii. Copy of Emergency Use Authorization for SinoPharm Covid 19 vaccine dated 26-10-2020 issued by National Health Regulatory Authority, Bahrain iii. Copy of Product Marketing Authorization Certificate dated 09-12-2020 issued by Ministry of Health & Prevention, UAE. iv. Weblink of official website of MOHAP, UAE regarding press release dated 09-12-2020 indicating official registration of said vaccine accessed on 08-01-2021. v. Weblink of official website of NMPA, China regarding press release dated 04-01-2021 indicating conditional approval for general use of said vaccine accessed on 08-01-2021.
	Pack size	1's PFS/ As per policy.
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	Not Available

Assessment by the Division of Biological Evaluation and Research

Initially, M/s Health Bee Projects Pvt. Ltd., Lahore applied for the registration of above-mentioned product. The case was discussed in 297th meeting of Registration Board wherein the Board decided as follows:

"Registration Board deferred the case for submission of following by the firm:

i. Original or Notarized Copy of Sole Agency Agreement.
ii. Evidence of approval of vaccine in vial in regulatory authorities along with web links of official websites confirming Registration/ Emergency Use Authorization.
iii. Clarification regarding provided real time stability data of 03 months for vial and 06 months for PFS while demanded shelf life is 24 months.
iv. *Updated accelerated stability data."*

The firm M/s Health Bee Projects Pvt. Ltd., Lahore has not yet submitted above documents, Moreover, now M/s National Institute of Health, Islamabad has submitted the same application with same dossier and submitted following additional documents:

i. A copy of letter (DO No.1/3/2021-Secy-NHS,R&C dated 14.01.2021) from Secretary, M/o NHSR&C dated 14-01-2021 addressed to Vice President, SinoPharm International, Beijing China wherein Maj. General Prof. Dr. Aamer Ikram, Executive Director, National institute of Health (NIH) has been nominated as focal person of M/o NHSR&C for communication with SinoPharm. Moreover, it has been informed to M/s SinoPharm International, China that DRAP has scrutinized clinical trial data on the BBIBP-CorV submitted by a third party. DRAP can issue the Emergency Use Authorization (EUA) for SinoPharm International or its Authorized Representative. The firm is further requested to resolve this issue urgently so that SinoPharm can be deployed for vaccination in Pakistan at the earliest **(Annex-I)**.

ii. A copy of letter from Maj. Gen. Prof. Dr. Aamer Ikram, Executive Director NIH (vide letter F.18(Gen)/2021-ED dated 15.01.2021) addressed to CEO, DRAP declaring that National institute of Health (NIH) will be the lead for this vaccine directly with SinoPharm China and DRAP as decided by the authorities further requesting to process application on their behalf **(Annex-II)**.

The application of M/s National Institute of Health, Islamabad is evaluated as per Form-5A and following deficiencies are observed:

i. Original or Notarized Copy of Sole Agency Agreement is not submitted. However following documents are provided:

   a. Copy of letter on the inclusion of COVID-19 Vaccine for Emergency Use (Trial) dated 23-07-2020 issued by The State Council's Joint Prevention and Control Mechanism for the COVID-19 Pandemic.

   b. Copy of Emergency Use Authorization for SinoPharm Covid 19 vaccine dated 26-10-2020 issued by National Health Regulatory Authority, Bahrain

c. Copy of Product Marketing Authorization Certificate dated 09-12-2020 issued by Ministry of Helath & Prevention, UAE

d. Weblink of official website of MOHAP, UAE regarding press release dated 09-12-2020 indicating official registration of said vaccine accessed on 08-01-2021.

e. Weblink of official website of NMPA, China regarding press release dated 04-01-2021 indicating conditional approval for general use of said vaccine accessed on 08-01-2021.

ii. Realtime stability data provided is of 06 months only while demanded shelf life is 24 months.

iii. Accelerated stability data provided is of 60 days.

The recommendations of Committee of experts for evaluation of clinical trial data for registration of COVID-19 vaccine is as under:

RECOMMENDATIONS OF COMMITTEE ON EVALUATION OF CLINICAL TRIALS

Recommendations of 3rd meeting of committee held on 31.12.2020

Third meeting of the committee of experts for evaluation of clinical trial data for registration of COVID-19 vaccines was held on 31.12.2020 at 2000 hours via zoom link. All the members and co-opted members attended the meeting. The committee after thread bare deliberation based on available clinical trial data and subsequent response to the queries by M/s SinoPharm, the committee recommended the following:

a. To grant EUA to COVID-19 vaccine of M/s Sinopharm, China (manufactured by Beijing Institute of Biological Products Co. Ltd) for use in population among people between 18-60 years age, including frontline workers and high-risk groups.

b. Adverse Events Following Immunization (AEFI) shall be mandatory part of approval through proper surveillance and record keeping.

c. Further consideration / approval for different populations / cohorts will be considered after submission of requisite peer reviewed clinical trial data.

Recommendations of 5th meeting of committee held on 07.01.2021

5th meeting of the committee of experts for evaluation of clinical trial data for registration of covid-19 vaccines was held on 07.01.2021 at 1900 hours via zoom link. All the members and co-opted members attended the meeting.

iv. The Committee considered the use of Sinopharm® vaccine in population with comorbidities. Members of the committee expressed their views based on their own experiences. It was resolved that use of the vaccine in patients with comorbidities should be based on a favorable

benefit/risk ratio. Immunocompromised individuals should not be administered the vaccine. The Committee feels that in case of any serious adverse events, disinformation campaign will be a very challenging issue and DRAP should evolve an efficient mechanism of Post Marketing Surveillance / AEFI.

Discussion:

Registration Board while discussing the matter of Sole Agency Agreement deliberated letters of Secretary, M/o NHSR&C to Vice President, M/s SinoPharm International, Beijing China and of Maj. Gen. Prof. Dr. Aamer Ikram, Executive Director NIH and decided to consider registration application submitted by NIH for grant of registration of SARS-CoV-2 Vaccine (Vero Cell), manufactured by M/s Beijing Institute of Biological Products Co., Ltd., China.

The Board was further apprised that M/s SinoPharm Pharm China has 2 manufacturing sites in China viz. M/s Beijing Institute of Biological Products Co Ltd and M/s Wuhan Institute and instant application is from Beijing Institute of Biological Products Co Ltd and same manufacturing site is also exporting to UAE as well

Registration Board also deliberated that said vaccine has already been granted Market Authorizations and Emergency use Authorizations in China, UAE and Bahrain.

Decision:

Keeping in view the above discussion, public health emergency, dire need of Corona Virus Vaccine and recommendations of the Committee on Evaluation of Clinical trials, Registration Board approved the SARS-CoV-2 Vaccine manufactured by M/s. Beijing Institute of Biological Products Co., Ltd., No. 6 & 9, Boxing 2nd Road, Economic-Technological Development Area, Beijing, 100176, China product for Emergency Use Authorization for active immunization of individuals between 18 to 60 years age, under Rule 29 (4) & (6) of the Drugs (Licensing, Registration & Advertising) Rules, 1976 subject to compliance of the following conditions:

i. **The vaccine should not be used in immunocompromised individuals and use of the vaccine in patients with comorbidities should be based on a favorable benefit/risk ratio.**
ii. **Firm shall ensure the strict compliance of Cold Chain (2^0C-8^0C) during transportation, storage and distribution cycle. The shelf life shall be twelve (12) months at 2^0C-8^0C.**
iii. **Emergency Use Authorization (EUA) shall be reviewed on quarterly basis keeping in view safety, efficacy and quality data of product.**
iv. **Firm shall ensure that terms and conditions of this registration will be made available to all relevant stakeholders (Government Agencies, Authorized distributors, Healthcare facilities, Healthcare providers etc.).**
v. **Firm shall submit data of Adverse Events Following Immunization (AEFI) to National Pharmacovigilance Centre, Pharmacy Services Division DRAP as per their requirement.**
vi. **Product shall be recalled in case of any quality issues or adverse reports regarding safety/ efficacy or as decided by Registration Board.**
vii. **The firm shall maintain complete records of distribution of vaccine.**
viii. **In case of any variation in the product profile and approval by Regulatory Authority of country of origin, the firm shall inform DRAP immediately.**
ix. **Approval letter will be issued after grant of DSL to NIH by relevant Licensing Authority.**

ANNEX-I

DO. No. 1/3/2021-Secy-NHS,R&C

GOVERNMENT OF PAKISTAN
MINISTRY OF NATIONAL HEALTH SERVICES,
REGULATIONS & COORDINATION

Islamabad the 14th January, 2021

SECRETARY

Mr. Yan Bing,
Vice President,
SinoPharm International
No. 20 Zhichun Road, Haidian District, Beijing,
China.

Subject: **COVID-19 VACCINE PROCUREMENT – SINOPHARM**

Excellency,

My gratitude to you and your team for a comprehensive briefing about SinoPharm's BBIBP-CorV Vaccine to Ministry of National Health Services, Regulations and Coordination (MNHSRC), Government of Pakistan at the National Command and Operation Center (NCOC) for COVID-19. We are pleased to follow up on agreed points from the meeting on 13th January, 2021.

2. Government of Pakistan reiterates its commitment to place an order for at least 1.1 million doses of BBIBP-CorV. Realizing the current stress on the BBIBP-CorV supply in the immediate future as discussed in our meeting today, we would appreciate an early indication of availability of a smaller quantity of the BBIBP-CorV in Q1 2021. This will would facilitate the inoculation drive for our critical front line healthcare workers.

3. MNHSRC's focal person for communication with SinoPharm is Maj. Gen. Prof. Dr. Aamer Ikram, Executive Director National Institute of Health (NIH). Please keep me copied in all communication. Contact details of the focal person is identified below:

Maj. Gen. Prof. Dr. Aamer Ikram
Official/Personal Email: edofficenih@gmail.com/ aamer.ikram@nih.org.pk
Telephone :+923215170713

4. As discussed in the meeting today, the Drug Regulatory Authority of Pakistan (DRAP) has scrutinized clinical trial data on the BBIBP-CorV submitted by a third party. DRAP can issue the Emergency Use Authorization (EUA) for BBIBP-CorV soon after receiving documentation/registration application from SinoPharm International or its Authorized Representative. We request, this issue to be addressed urgently so that SinoPharm can be deployed for vaccination in Pakistan at the earliest.

5. We look forward to a fruitful collaboration between Government of Pakistan and SinoPharm International.

Kind regards

14/01/2021

(Aamir Ashraf Khawaja)
Secretary
Official email: secretary@nhsrc.gov.pk
Personal email: paki002@yahoo.com
Telephone: +92 3324666456

Kohsar Block, 3rd Floor, Constitution Avenue, Islamabad. Ph. # 92-51-9245811 Fax # 92-51-9245812

MOST URENT

F.18 (Gen)/2021-ED
NATIONAL INSTITUTE OF HEALTH
Ministry of National Health Services, Regulations & Coordination
Ph: (92-051) 9255117 Fax: (92-051) 9255099 Email: edofficenih@gmail.com
National Focal Point for International Health Regulations

15 January 2021

The Chief Executive Officer (CEO)
Drug Regulatory Authority of Pakistan
TF Complex G-9/4
Islamabad

Subject: **Registration of SinoPharm Vaccine**

The complete application regarding SARS-CoV-2 (Vero Cell), inactivated vaccine manufactured by Beijing Institute of Biological Products Co., Ltd. China has already been submitted for formal approval of DRAP for emergency use authorization.

2. National Institute of Health (NIH) will be the lead for this vaccine directly with SinoPharm China and DRAP as decided by the authorities.

3. Kindly process the application on our behalf.

Major General
Prof. Dr. Aamer Ikram, SI(M)
Executive Director

Copy to:

1. National Command and Operation Centre (NCOC), Islamabad
2. The Special Assistant to Prime Minister on Health, Ministry of National Health Services Regulations & Coordination, Islamabad
3. The Secretary, Ministry of National Health Services Regulations & Coordination, Islamabad
4. The Director General Health, Ministry of National Health Services Regulations & Coordination, Islamabad

2. M/s AJM Pharma (Pvt) Ltd., Karachi.

Following product of M/s AJM Pharma (Pvt) Ltd., Karachi was deferred in 297th meeting of Registration Board as per following details:

Name of Applicant	M/s AJM Pharma (Pvt) Ltd 115, Industrial Triangle, Kahuta Road, Islamabad.
DSL details	DSL License No.1016 valid upto 18-06-2021. **Address**: M/s AJ Mirza Pharma (Pvt.) Ltd. 1st floor, Shafi Court Civil Lines, Merewether Road, Karachi. **Address of Godown**: floor, Shafi Court Civil Lines, Merewether Road, Karachi.
Name of Manufacturer	CanSino Biologics 185 South Street, TEDA, Tianjin 300457, People's Republic of China Zip code: 300457
Brand Name + Dosage Form + Strength	**Convidecia** Vaccine Replication-defective recombinant human type-5 adenovirus expressing S protein of novel coronavirus, 5 x 10^{10}vp
Composition	Eeach 0.5ml dose contains: Recombinant Novel Coronvirus Vaccine (Adenovirus Type 5 Vector)
Finished product specifications	Finished Pharmaceutical Product Import
Shelf life	24 Months (Store at 2°C to 8°C)
International availability	Not submitted any registration Certificate
Alternate Products already registered in Pakistan	No alternate available.
Type of Form Dy. No. Date of Application, Fee submitted	Dy.No.32828(R&I) DRAP Dated 9-12-2020. Fee: 50,000/- Dated 08-12-2020.
Demanded Price Pack size	As per SRO/ 0.5mL prefilled syringe
General Documentation	1. Photocopy of Letter of Authorization dated 04-01-2021. 2. Photocopy of Certificate of Good Manufacturing Practice (GMP) issued by China Food and Drug Administration on 29-08-2018. 3. Photocopy of Approval Letter of Military Specifically-Needed Drugs dated 25-06-2020. **(on letter head of Health Bureau of Logistics Support Department of central Military Commission)**
Decision of RB in 297th meeting	*Registration Board deferred the case for submission of following by the firm:* *i. Clarify of two DSL (i.e. in the name of AJM and AJ Mirza) issued at same address.* *ii. Copy of Registration Certificates. Web links of official websites of any regulatory authority confirming Registration/ Emergency Use Authorization.* *iii. Clarification why accelerated stability data of three batches do not comply to the specification in 3rd month.*

	iv. Clarification regarding provided real time stability data of 09 months & 06 months while demanded shelf life is 24 months. **v.** *Phase-III Clinical Study (Safety and Efficacy) Report.*

The firm has now submitted the following documents:

i. Both DSL are issued at same address as warehouses of both companies are located at same floor but at different designated area. Please note that AJM Pharma is solely import based company and its NTN registration number is 4097489 and DSL number is 1016.

ii. Ad5-nCoV manufactured by CanSinoBio is in process of rolling submission to Chinese regulatory authority NMPA for conditional approval. Ad5-nCOV vaccine has received approval for military use in China (attached). No web links is available at this time.

iii. In the manufacturing process development, we scaled up the manufacturing process to 200L batch-fed mode and then continued to 50L perfusion mode to increase the yield. After process improvement and further scale up, stability studie of more lots of drug product have been initiated and they are ongoing at present time. We have one lot of drug product packaged in PFS which is stable at 25 ± 2^0C for 3 months and we have stability data showing that the product in glass vials are stable for 9 months at $2\text{-}8^0$C. We are accumulating more data on the stability studies.

iv. Copy of commitment of M/s CanSino Biologics Inc. to provide the complete stability profile to DRAP in the future. If there is any non-compliance to specification during shelf life of the registration batches, CanSinoBio will inform DRAP.

v. Copy of commitment of M/s CanSino Biologics Inc. to provide interim analysis results to DRAP as soon as possible

The recommendation of Committee of experts for evaluation of clinical trial data for registration of COVID-19 vaccine is not available for this vaccine.

Decision:

Registration Board deferred the case till the availability of Phase-III clinical trial data and its evaluation by Expert Committee for Evaluation of Clinical Trial Data and rectification of shortcomings in registration dossier by the applicant.

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