MINUTES OF 299th MEETING OF REGISTRATION BOARD HELD ON 22nd JANUARY, 2021

299th meeting of Registration Board was held on 22nd January, 2021 in the Committee Room of Drug Regulatory Authority of Pakistan, G-9/4, Islamabad. The meeting was chaired by Dr. Obaidullah, Director, PE&R/ Chairman Registration Board. 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.

4.	Lt. Gen. (R) Dr. Karamat Ahmed Karamat HI-M, SI-M, Former Surgeon General Pakistan	Member
5.	Dr. Rafeeq Alam Khan, Meritorious Professor, Faculty of Pharmacy, Ziauddin University, Karachi	Member
6.	Maj.Gen. (R) Dr. Tahir Mukhtar Sayed, Inspector General (Hospitals), Fauji Foundation, Rawalpindi	Member
7.	Dr. Qurban Ali, Ex-Director General, National Veterinary Laboratories, Islamabad	Member
8.	Mr. Iftikhar A.Choudhary, Hospital Pharmacist, Lahore	Member
9.	Dr. Khalid Javed Director DTL Peshawar	Member
10.	Mr. Muzammil Waheed Director DTL Rawalpindi	Member
11.	Mr. Ghulam Mujtaba, Representative of IPO, Islamabad.	Member

Prof. Brig. (R) Dr. Muzammil H. Najmi, Chairman Committee on Evaluation of Clinical Trials and Mr.Shahid Malik Additional Secretary Drugs Control, Department of Health Punjab also joined the meeting via zoom link.

Dr. Amanullah Khan director DTL, Quetta and Muhammad Aslam Representative of M/o Law & Justice could not attend the meeting but lately endorsed decision of Registration Board through WhatsApp.

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 AGP Limited, Karachi

1.	**Name and address of Importer**	M/s AGP Limited, B-23-C, S.I.T.E., Karachi.
	Detail of DSL	DSL No. 002 dated 13-11-2020 valid till 21-09-2021
	Name and address of Manufacturer	**Manufacturer & Quality Control:** Medgamal Branch, FSBI N.F. Gamaleya "National Research Center for Epidemiology and Microbiology" of the Ministry of Health of the Russian Federation, 18 Gamalei Street, Moscow 123098, Russia.
	Brand Name +Dosage Form + Strength	Gam-COVID-Vac Combined vector vaccine for the prevention of coronavirus infection caused by the SARS-CoV-2 virus Solution for Intramuscular Injection
	Diary No. Date of R& I & fee	Dy. No. 2086, 2273, 2316, 2450 (R&I)&209 (Dir. Bio) dated 18-01-2021, 19-01-2021, 20-01-2021, 21-01-2021& 22-01-2021 Rs. 50,000/- Dated 18-01-2021 Rs. 50,000/- Dated 19-01-2021
	Composition	**Component I:** Each dose of 0.5ml in vial contains: Serotype 26 recombinant adenovirus particles containing SARS-CoV-2 protein S gene ……..$(1.0 \pm 0.5) \times 10^{11}$ particles **Component II:** Each dose of 0.5ml in vial contains: Serotype 5 recombinant adenovirus particles containing SARS-CoV-2 protein S gene ……..$(1.0 \pm 0.5) \times 10^{11}$ particles
	Pharmacological Group	Corona Virus Vaccine
	Type of Form	Form-5A
	Finished Product Specification	In-House
	Shelf Life	6 months for both components ($\leq -18^0$C)
	Pack size	1's (1 Vial of Component I in Card box + 1 Vial of Component II in Card box)
	Method of Administration	• The vaccine is intended for intramuscular injection only. Intravenous injection of the product is strictly prohibited. The vaccine is injected into the deltoid muscle. The vaccination is carried out in two stages: first with component I, then 3 weeks later with component II. • Before the injection, the product (component) must be removed from the freezer and kept at room temperature until completely thawed for not more than 30 minutes, stir before use by gently shaking the vial. It is not allowed to shake the product sharply. • Storage of the opened vial is not allowed. • Re-freezing of the preparation is not allowed.
	Reference Regulatory Authority Availability	Not Available
	Products already registered in Pakistan	Not Available

Assessment by the Division of Biological Evaluation and Research

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.

The firm has submitted following documents in support of their application:

i. Translated copy of Provisional registration dated 15-12-2020 valid till 15-12-2021 Issued by Republic of Belarus along with weblink of official website of Belarus
ii. Translated copy of Registration Certificate of Drug for Medical Application dated 11-08-2020 valid till 01-01-2021 issued by Russia along with weblink of official website of Russia
iii. Translated copy of Amended Registration Certificate of Drug for Medical Application dated 30-12-2020 valid till 01-01-2022 issued by Russia.
iv. Translated copy of Emergency Use Authorization dated 10-01-2021 valid till 01-10-2022 issued by Palestine.
v. Copy of press release dated 23-12-2020 issued by Argentine regarding Emergency Authorization of Sputnik V vaccine along with weblink of official website.
vi. Pakistan Notarized Copy of letter of exclusive authorization has been issued by First Deputy CEO of "Russian Direct Investment Fund" **(RDIF)**dated 08-11-2020 in name of M/s Aurugulf Health Investment-Sole Proprietorship LLC, Abu Dhabi, UAE for many countries including Pakistan.
vii. Pakistan Notarized Copy of letter of appointment dated 15-01-2021 issued by M/s Aurugulf Health Investment, Abu Dhabi, UAE in name of Private office of His Highness Sheikh Ahmed Dalmook Al Maktoum, 27th floor Burj Al Salaam tower, Sheikh Zayed Road, Dubai, UAE regarding sale and distribution in Pakistan.
viii. Pakistan Notarized Copy of Letter of Authorization dated 19-01-2021 issued by Private office of His Highness Sheikh Ahmed Dalmook Al Maktoum, 27th floor Burj Al Salaam tower, Sheikh Zayed Road, Dubai, UAE appointing M/s AGP Limited, B-23, S.I.T.E., Karachi to Register/ Market/ Sale/ Tender Business of Gam-COVID-Vac in Pakistan.
ix. The firm has submitted an undertaking that the data in Form-5A and all letters of authorizations provided in the dossier are correct and true as per their knowledge and for any false claim or document, company M/s AGP Limited, Karachi will be responsible.
x. The firm has submitted real time stability data (-18^0C to -22^0C) of three series of both components for 08 months.
xi. The firm has not submitted accelerated stability data and informed that the manufacturer has developed a new stability program ensuring stability at $2\text{-}8^0$C with 2 months study. The document is not officially released yet until approved by Russian regulators. The approval is expected in current month. They will submit the document as they receive from their principal.

RECOMMENDATIONS OF COMMITTEE ON EVALUATION OF CLINICAL TRIALS

Recommendations of 5th meeting of committee held on 07-01-2021

Clinical trial data of Sputnik-V vaccine manufactured by Gamaleya was discussed in 05th meeting of Committee held on 07-01-2021 wherein the Committee decided as follows:

a. The manufacturer has reported completion of their trial in a Press Release. They may be asked to provide complete/recent data of the trial.
b. The manufacturer may be asked to provide information on location of the contact dermatitis noted with their vaccine i.e. whether it was restricted to the site of administration only or affected other areas of body as well.

Recommendations of 7th meeting of committee held on 08-01-2021

a. The committee discussed the response provided by the firm M/s Gamaleya National Center of Epidemiology and Microbiology, Russia

b. The committee deliberated that percentage of contact dermatitis is more than 20 percent, which is worrying as it is significantly higher in vaccinated group. The committee further deliberated that we should wait for the complete data and should hold EUA till final report particularly completion of ADR report, as per response of the firm that complete report will be published in next few weeks.

Recommendations of 8th meeting of committee held on 21-01-2021

The committee in its 8th meeting held on 21-01-2021 discussed data of 2nd interim analysis submitted for Sputnik V vaccine manufactured by M/s Gamaleya National Center of Epidemiology and Microbiology, Russia in response to queries raised in the 7th meeting of committee held on 14.01.2021.

On the basis of the available information/data, the Committee recommends Sputnik V vaccine manufactured by M/s Gamaleya National Center of Epidemiology and Microbiology, Russia for granting Emergency Use Authorization in people above 18 years of age, including the people over 60 years of age and those with co-morbidities.

Proceedings of Registration Board:

During meeting, Chairman Registration Board asked every member for their questions/ queries regarding above mentioned vaccine. Dr. Qurban Ali apprised the Board that Adenoviruses are long studied viruses and have well established safety profile. Moreover, he emphasized mentioning word "frozen" on the label of the vaccine. Dr. Qurban Ali further apprised the Board that the said vaccine is a novel vaccine using two different types of adenoviruses in two components of the same vaccine. He further submitted that in future the same technology will be used for vaccine development. Moreover, CanSinoBio and Johnson & Johnson have also used Adenoviruses in their vaccines' development. Hence, DBE&R needs to be more vigilant in such vaccines. Mr. Muzammil Waheed also agreed with the Dr. Qurban Ali. One of the members raised the query regarding the adverse events of the vaccine during trial. Prof. Brig. (R) Dr. Muzammil H. Najmi responded the query and apprised the Board that adverse events observed during the period are common, mild and usually observed in other vaccines as well. Another member raised query about the contact dermatitis observed in vaccinated individuals during trial. Prof. Brig. (R) Dr. Muzammil H. Najmi responded the query and apprised the Board that in 1st interim report, the contact dermatitis was more than 20%, however, in 2nd interim report the data shows that the contact dermatitis is not significant.

Registration Board was further apprised that Embassy of Russian Federation has written a letter to CEO, DRAP on 1901-2021 informing that all the data on Russian vaccine Sputnik V required for Emergency Use Authorization has been submitted to DRAP. In case of grant of EUA, the Russian side will be able to supply 25,000 to 100,000 doses of Sputnik V in January and meet the demand of Pakistan in full within 4 to 6 months.

Registration Board further discussed that as multiple companies are involved in sale and distribution authorization of said vaccine, so it will be more appropriate to get further verification regarding the sole agency authorization for territory of Pakistan. It was discussed that as Embassy of Russian Federation has requested for

grant of EUA for Sputnik V vaccine, therefore Embassy of Russian Federation may be requested to verify the sole agent authorization of said vaccine in Pakistan before issuance of Emergency Use Authorization. All the members of the Board agreed with the grant of Emergency Use Authorization subject to said verification from Embassy of Russian Federation.

Decision:

Keeping in view the public health emergency, dire need of Corona Virus Vaccine and recommendations of the Committee on Evaluation of Clinical trials, Registration Board approved the product for Emergency Use Authorization for active immunization of individuals ≥ 18 years age under Rule 29 (4) & (6) of the Drugs (Licensing, Registration & Advertising) Rules, 1976 subject to compliance of the following conditions:

i. **Authorization shall be reviewed on quarterly basis keeping in view safety, efficacy and quality data of product.**
ii. **The vaccination is carried out in two stages: first with component I, then 3 weeks later with component II.**
iii. **The shelf life of the unopened vials shall be (06) months at ≤ -18^{0}C and storage of opened vial and re-freezing is not allowed.**
iv. **Firm shall ensure the strict compliance of temperature conditions (≤ -18^{0}C) during transportation, storage and distribution cycle.**
v. **Firm shall ensure that terms and conditions of this EUA-registration will be made available to all relevant stakeholders (Government Agencies, Authorized distributors, Healthcare facilities, Healthcare providers etc).**
vi. **Firm will submit data of Adverse Events Following Immunization (AEFI) to National Pharmacovigilance Centre, Pharmacy Services Division DRAP.**
vii. **The firm shall maintain complete records of distribution of vaccine.**
viii. **Product shall be recalled in case of any quality issues or adverse reports regarding safety/ efficacy or as decided by Registration Board.**
ix. **In case of any variation in the product profile and approval by Regulatory Authority of country of origin, the firm will inform DRAP immediately.**

Registration Board further decided that as multiple firms are involved in grant of Sole Agency Authorization to M/s AGP Ltd., Karachi therefore documents submitted by M/s AGP Ltd., Karachi regarding sole agency will be forwarded to Embassy of Russian Federation in Pakistan with request to verify their authenticity for nominated sole agent of above vaccine in Pakistan. After aforementioned confirmation, case will be processed for approval by Chairman Registration Board for issuance of Emergency Use Authorization.