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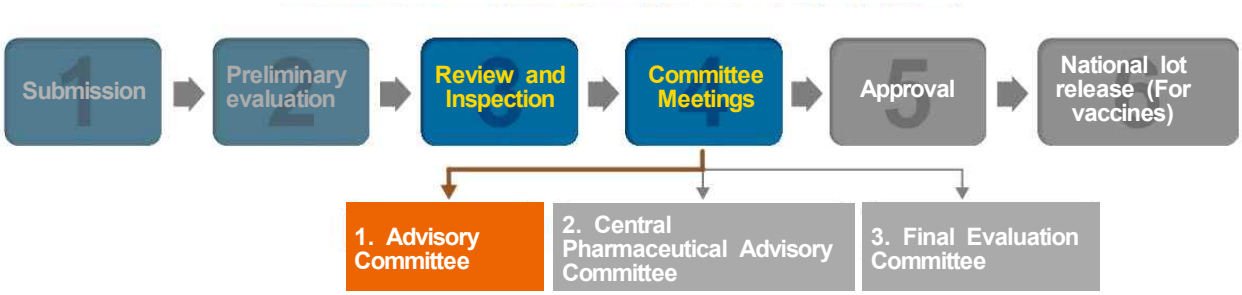
		Division	· Biopharmaceuticals and Herbal Medicine Bureau · Biopharmaceutical Policy Bureau · Novel Products Approval Office · Overall Evaluation Team, Vaccine Review Division, COVID-19 Emergency Response Support Headquarters · Clinical Review Team, Vaccine Review Division, COVID-19 Emergency Response Support Headquarters
Ministry of Food and Drug Safety		Director	· 김춘래 (☎043-719-3302) · 정현철 (☎043-719-5351) · 김희성 (☎043-719-5061) · 강주혜 (☎043-719-4151)
		Deputy Director & Researcher	· 김지연 (☎043-719-3311) · 남주선 (☎043-719-5354) · 김지현 (☎043-719-5063) · 왕소영 (☎043-719-3077)

Advisory Meeting Outcomes on Moderna COVID-19 Vaccine

1 Current Marketing Authorization Review Status



☐ On May 9, the Ministry of Food and Drug Safety (MFDS, Minister Kim Ganglip) convened a meeting of the COVID-19 Vaccine Safety and Clinical Efficacy Advisory Committee (hereinafter “the Advisory Committee”) to review the clinical trial results of the Moderna COVID-19 vaccine of Green Cross Corporation, or GC Pharma.

○ The Advisory Committee meeting is a mandatory procedure to seek multidisciplinary experts’ consultations on clinical, nonclinical and quality data before consulting with the Central Pharmaceutical Advisory Committee.

- For the Moderna vaccine review, the Advisory Committee meeting was

attended by seven experts in areas such as infectious diseases, vaccine, and clinical data.

2 Clinical Trial Results and Committee Meeting Outcomes

<< Overview >>

☐ The clinical trial data submitted by GC Pharma included the interim results of ongoing phase I·II·III clinical trials (one each) conducted in the United States; and the vaccine's safety and efficacy was reviewed mostly based on the phase III clinical trial conducted in the US.

○ In the phase III clinical trial, 30,351 participants with an average age of 52 were administered with either the test vaccine or placebo. Among the participants, 47.3 percent (or 14,366 participants) were women; 22.5 percent (or 6,817 participants) had underlying diseases such as obesity, lung diseases or diabetes; and 24.8 percent (or 7,520 participants) were aged 65 and older.

<< Efficacy >>

☐ **(Preventive Effect)** The effectiveness in prevention was evaluated by giving two doses of either the test vaccine or placebo (0.9 percent saline solution) to 28,207 participants (14,134 in the vaccinated group and 14,073 in the control group) who had not been tested positive for COVID-19.

○ The preventive effect was evaluated based on the comparison and analysis of the percentage of COVID-19 cases in each group 14 days after two doses of vaccination with a 28-day interval. Participants were considered infected when they showed clinical symptoms for COVID-19 and were tested positive following a *RT-PCR** test for SARS-CoV-2.

* RT-PCR (Reverse Transcription Polymerase Chain Reaction): Abbott Real Time SARS-CoV-2 RT- PCR assay

○ According to the evaluation, the vaccine showed an *efficacy rate** of approximately 94.1 percent with 11 confirmed cases in the vaccinated group and 185 in the placebo group 14 days after the second dose of vaccination.

Regardless of the participants' age[1] or underlying disease[2], the vaccine demonstrated an efficacy rate of 86 percent or more.

* Efficacy rate (%) = 100 x (1 - (percentage of confirmed cases in the vaccinated group) / (percentage of confirmed cases in the control group))

Category		Efficacy rate (%)
		14 days after second dose
Age[1]	between 18-64	95.6
	65 or more	86.4
Underlying disease[2]	With	90.9
	Without	95.1

* according to domestic and international standards (e.g. WHO) on the evaluation of COVID-19 vaccines' efficacy (an efficacy rate of 50 percent or more)

○ For severe cases or deaths from COVID-19 infection, 31 cases were reported in the control group (30 severe cases and 1 death) and none in the vaccinated group.

□ **(Immunogenicity Evaluation)** As an indirect indicator of the vaccine's efficacy, immunogenicity was evaluated by examining the kind and amount of antibodies generated in the body after vaccination.

* Immunogenicity evaluation was based on two (2) clinical trials, or phase I·II clinical trials (one each) conducted in the United States.

○ In terms of neutralizing antibodies which affect efficacy by attaching to a viral particle surface and thereby neutralizing viral infectivity, the seroconversion rate, or the percentage of participants whose antibody titer increased fourfold or more after 4 weeks from the second dose of vaccination, was 100 percent compared to pre-vaccination.

□ **(Consultation results)** The Advisory Committee noted that the submitted data proved the vaccine's efficacy 14 days after the second dose of vaccination in people aged 18 and older, concluding that the vaccine's preventive effect is acceptable for an authorization.

<< Safety >>

☐ 30,342 participants (15,179 in the vaccinated group; 15,163 in the control group) were monitored for s*olicited adverse events** following immunization (*local and systemic***) for the first seven days after vaccination.

* Solicited adverse events: during the initial days (or within the first seven days) after vaccination (either dose), adverse events were actively monitored using an electronic system where a list of adverse events following immunization were recorded.

** (local) pain at the injection site, redness, swelling and lymphadenopathy (systemic) headache, fatigue, muscle pain, joint pain, nausea, fever and chills

○ The local symptoms included pain at the injection site (92.0 percent), lymphadenopathy (19.8 percent), swelling (14.7 percent) and redness (10.0 percent), which were mostly mild to moderate symptoms and disappeared within one to three days from the onset.

○ The systemic symptoms included fatigue (70.0 percent), headache (64.7 percent), muscle pain (61.5 percent), joint pain (46.4 percent), chills (45.4 percent), nausea (23.0 percent) and fever (15.5 percent), which were mostly mild to moderate symptoms, appeared within one to two days from vaccination and disappeared within one to two days from the onset.

○ For most of the local and systemic symptoms, people aged 65 and older reported lower frequency and severity compared to other adults.

☐ Vaccination-related unsolicited adverse events (monitored for 4 weeks after vaccination) were reported by 8.2 percent of the vaccine recipients (1,242/15,185 participants); their major symptoms included fatigue (1.5 percent), headache (1.4 percent), muscle pain (0.8 percent), pain at the injection site (0.8 percent) and redness at the injection site (0.8 percent).

* Unsolicited adverse events: adverse events voluntarily reported by participants during a medical checkup or by telephone in the first four weeks after vaccination

○ Adverse events among elderly participants were similarly reported compared to other adults.

* adult participants (aged from 18 to 64): 8.2 percent (938/11,415 participants) reported vaccination-related unsolicited adverse events

* elderly participants (aged 65 and older): 8.1 percent (304/3,770 participants) reported

vaccination-related unsolicited adverse events

○ Among the 30,351 participants registered in the clinical trials, serious adverse events were reported in 1.0 percent of the vaccinated group (147 participants) and 1.0 percent of the control group (153 participants); and there were *nine (9)** serious adverse drug reactions such as facial swelling, of which a causal relation with vaccination cannot be excluded, while most of the patients recovered at the time of clinical data submission.

* facial swelling (2), nausea (1), vomiting (1), rheumarthritis (1), autonomic dysfunction (1), peripheral oedema (1), dyspnoea (1), B-cell lymphoplasmacytic lymphoma (1)

□ **(Consultation results)** Regarding the adverse events reported during the clinical trials, the Advisory Committee concluded that the vaccine had an acceptable safety profile.

○ The Committee also advised that there should be a Risk Management Plan (RMP) to monitor and follow up on the adverse events that were reported during the clinical trials to ensure post-authorization safety.

3 Future Plans for Review and Approval

□ MFDS will continue to make every effort to guarantee rigorous review and approval processes for COVID-19 vaccines and treatments and at the same time ensure objectivity and transparency across all regulatory processes by heeding expert opinions from diverse fields.

○ After assessing the submitted data (e.g. quality data) of GC Pharma's Moderna COVID-19 vaccine, the Ministry will take into account the consultations and recommendations from the Advisory Committee as well as the assessment results. Based on these, MFDS will convene a Central Pharmaceutical Advisory Committee meeting on Thursday, May 13, to seek advice on product safety, efficacy and pre-authorization considerations before announcing the meeting outcomes in the afternoon the same day.