Study on the efficacy and safety of the H5N1 highly pathogenic avian influenza A/Ezo red fox/Hokkaido/1/2022 (NIID-002) national stockpile vaccine (prototype)

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The Japanese government has been stockpiling pre-pandemic vaccines against viruses with pandemic potential since 2006. The National Action Plan for Pandemic Influenza and New Infectious Diseases, enacted in 2013, emphasizes the importance of this stockpile in preparation for future outbreaks. According to the vaccination guideline prepared under the plan, in the event of a novel influenza outbreak, the strain of the virus with the highest expected efficacy should be selected from the stockpile. Additionally, cross-reactivity should be assessed using serum from individuals who received pre-pandemic vaccines to ensure efficacy against circulating viruses.

Considering that circulating wild-type H5 subtype viruses belonged to clade 2.3.4.4b and that H5 viruses detected in mammals in Japan were H5N1, A/Ezo red fox/Hokkaido/1/2022 (NIID-002) was selected as the vaccine strain for 2024 and 2025 at the Subcommittee meetings on Countermeasures for Novel Influenza under the Health Sciences Council.

During a pandemic, marketing authorization will be expedited. It is important to note that, as the prototype vaccines formulated for the national stockpile are unlicensed products during non-epidemic periods, there is no prior experience with the administration of the vaccine to humans. Previous clinical trials, including investigator-initiated trials, using H5N1 and H7N9 vaccine strains, have revealed that immunogenicity varies between strains. Furthermore, extrapolation using nonclinical studies with ferrets has proven difficult. These factors underscore the need for clinical trials and human immunogenicity data. In addition, it is crucial to preserve remaining serum for future evaluation of cross-immunity with epidemic strains and vaccine efficacy when HPAIV outbreaks occur.

In light of these considerations, this study is conducted as an open-label phase II investigator-initiated clinical trial with the following objectives:

1) to assess the efficacy and safety of pre-pandemic vaccines stockpiled under the National Action Plan for Pandemic Influenza and New Infectious Diseases, in line with the Act on Special Measures against Novel Influenza, etc.,

2) to store serum samples from pre-pandemic vaccine recipients at the National Institute of Infectious Diseases (NIID) for exploration of cross-immunity using the serum in the event of a novel influenza outbreak, and

3) to compare the immunogenicity of other novel influenza vaccine modalities using the stored serum. In addition to evaluating the stockpiled vaccine's efficacy and safety, storing the remaining serum at NIID will enable future studies on cross-immunity with epidemic strains

and HPAIVs. Moreover, comparisons with mRNA and recombinant vaccines under development will provide important evidence for countermeasures against emerging influenza strains.