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**ADAPTING FLUBLOK/SUPEMTEK® RECOMBINANT PROTEIN EXPRESSION SYSTEMS TO SARS-COV-2**

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Sanofi co-developed a SARS-CoV-2 recombinant protein vaccine for the prophylaxis of COVID-19 disease based on recombinant protein antigens adjuvanted with AS03 from GSK. The recombinant protein used leverages the safe and effective platform used to produce Flublok/Supemtek® (Flublok), the first licensed recombinant seasonal influenza vaccine. The manufacturing process of Flublok utilizes a platform based on the baculovirus expression vector system (BEVS) for the expression of recombinant hemagglutinin (rHA) proteins in insect cells. Recombinant proteins in this system are expressed using a viral vector (baculovirus Autographa californica multinucleocapsid nuclear polyhedrosis virus) that is non-pathogenic to humans. Our cell line for protein expression is a non-transformed, non-tumorigenic continuous insect cell line expressSF+® (SF+) that is derived from Spodoptera frugiperda. Once expressed, recombinant proteins are purified, formulated and filled. A schematic of this process is shown in Figure 1.

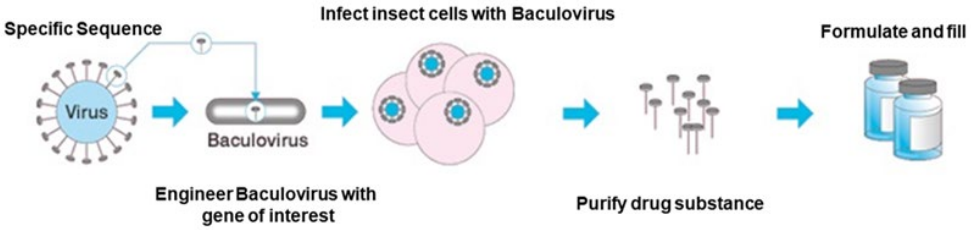


*Figure 1. A schematic of the BEVS production platform.*

The Sanofi recombinant protein subunit of the SARS-CoV-2 vaccine contains purified recombinant prefusion Spike protein (preS dTM)1; based on the NCBI Reference Sequence YP_009724390.1 (D614) and modified to improve the conformation, stability, trimerization and to facilitate purification2. The Flublok process, materials, and tests were leveraged to the greatest extent possible to facilitate development and production of preS dTM, see Figure 2.

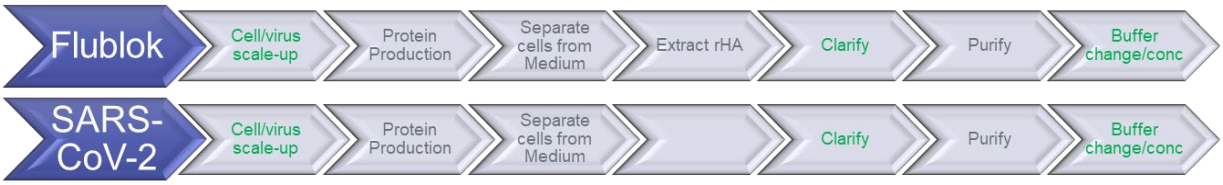


*Figure 2. Process Flow Diagrams. Steps shown in green are similar between the Flublok and SARS-CoV-2 processes.*

Using this strategy, we manufactured the first clinical GMP SARS-CoV-2 drug substance batch of drug substance less than 4 months after acceptance of the antigen gene sequence. Post validation and industrialization of the current D614 process, the production of Beta variant (B.1.351) antigen was accelerated using methodology adapted from our typical Flublok ® strain change process. These antigens are highly purified, have been extensively characterized and used in multiple clinical trials, including bivalent and booster studies1,2,3,4.

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1. Goepfert PA, Fu B, Chabanon AL, et al. Lancet Infect Dis 2021; 21: 1257–70.
2. Sanofi Pasteur Inc. Vaccines Against SARS-COV-2 Infections. WIPO WO 2022/046634. 2022.
3. Sridhar S, et al. Lancet Infect Dis 2022;S1473-3099(21)00764-7.
4. https://clinicaltrials.gov/ct2/show/NCT04904549