

# Participation in ENSEMBLE phase III multicenter clinical trial of Ad26.CoV2.S, a COVID-19 vaccine: An investigational drug services perspective

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## Funding information

Janssen Pharmaceuticals, Titusville  
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## Abstract

**What is known and objective:** Since WHO declared the pandemic of COVID-19, vaccines have been developed to fight against this infectious disease. Coordination and participation of investigational drug services to facilitate a phase III COVID-19 vaccination clinical trial are described and discussed, with novel interventions coordinating the dispensing processes in the trailer settings.

**Comment:** Once the study has reached phase III, the large number of participants and fast enrolment would contribute to the vaccine development.

**What is new and Conclusion:** The investigational drug service (IDS) performed responsibilities in clinical and trailer units, and minimized workflow disturbances to maximize validity during the dispensing process. The advantages of mobile units and trailers increase flexibility of participants, broaden service area and improve feasibility, especially in minority and underserved communities. The UCM IDS team performs responsibilities in both clinical and mobile unit settings, the IDS team is able to facilitate and expand the enrolment to the minority population in underserved communities.

## KEYWORDS

controlled clinical trial, COVID 19, ENSEMBLE trial, investigational drug service, vaccine

## 1 | WHAT IS KNOWN AND OBJECTIVE

Since the first reported case of COVID-19 in December 2019, an urgent global quest for effective therapies to prevent and treat the virus has been ongoing. Rapidly developing a vaccine to prevent the spread of COVID-19 was an imperative.<sup>1</sup> By the end of July 2020, there were already 139 vaccines in preclinical development and 27 potential vaccines in clinical evaluation.<sup>2</sup> Among the varied types of vaccines, the majority of research laboratories and pharmaceutical companies have based their COVID-19 vaccine developments on three strategies to specifically target the rapid mutation rate of SARS-CoV-2: (a) a nucleic acid-based vaccine,<sup>3</sup> (b) a traditional recombinant vaccine expressing the spike (S) protein,

and (c) a replicating or non-replicating viral vector vaccine. Janssen Pharmaceuticals, in particular, had developed a COVID-19 vaccine based on a replication-competent vector that induced a robust, likely durable immune response with a single dose, similar to the Ebola vaccine.<sup>4</sup> With the successfully conducted trial, the Food and Drug Administration (FDA) had approved Emergency Use Authorization of Janssen COVID-19 vaccine.

As a crucial element of the Department of Pharmacy, the Investigational Drug Services (IDS) team at the University of Chicago Medicine (UCM) worked closely with the office of clinical research at the university to conduct the ENSEMBLE trial. The purpose of this article is to share, from a pharmaceutical perspective, the experience of participating in Janssen's phase III clinical ENSEMBLE

trial of the SARS-CoV-2 vaccine study at one of its testing sites and introduce a novel intervention that streamlined the procedure. In order to increase participant flexibility, broaden the service area, and create easier access, especially in minority and underserved communities, the IDS pharmacy team participated in designing the pharmacy practice area in mobile units in the ENSEMBLE phase III trial. This paper discusses the usefulness of this approach and provides information on how to maintain compliance and manage the investigational product at mobile unit settings while still maintaining protocol compliance.

## 2 | COMMENT

Transitioning a full clinic to a mobile clinic in a trailer setting can be challenging and requires an extensive amount of planning. Prior to relocating into the trailer setting, the IDS pharmacy team ensured that the following essentials were present in each mobile unit: a refrigerator for proper vaccine storage, hospital network with an encrypted Internet connection to access a web-based medical records system, portable printer for participant prescription labels, biosafety cabinet for sterile medication preparation and ventilation, sterile compounding supplies and personal protection equipment (PPEs).

The investigational drug, placebo and ancillary supplies were transferred from the main clinic to the trailer on a daily basis for maximum security reasons. The temperature during the transportation process was constantly monitored by placing a digital temperature recorder next to the vaccine box. Pharmacy staff would condition the certified cooler and “sandwiching” the vaccines with temperature logger in between ice packs in the cooler. Based on temperature log readings throughout the workday, we were successfully able to maintain the required 2–8°C during the transportation process. After arriving at the trailer unit, pharmacy personnel would immediately transfer the vaccine, temperature logger and ice packs into the fridge in the trailer units. At the end of the day, the same “sandwich” packaging was applied when returning the study vaccine to the medical centre building.

General Internet and encrypted hospital network were established before the team initiated the first participant of the study. The network connection ensured that the study team, including pharmacy personnel, continued the same practice procedures in the trailer as in the clinic setting. These procedures included, but were not limited to, screening and enrolling participants via Interactive Web Response Systems (IWRS), medication order verification, and investigational product assignment via IWRS. Although the health-care field has transitioned in recent years to rely quite heavily on Internet communications for fast and accurate data records and transfer, the use of mobile units still necessitates paper-based documentation as a backup to prepare for emergencies, such as an interrupted Internet connection. A backup plan was established to maintain proper workflow under any potential circumstances; in requiring physicians to use paper forms to place an order, pharmacists in the trailers had to communicate with the staff in the main clinic to

clarify the randomization group for a certain participant. After randomization had been assigned, the pharmacists in the trailer would start preparing and labelling the dose with pre-printed labels that were designed to provide study-specific information (site number, physician, placebo or vaccine) and fill participant-specific information manually (eg participant name, ID, DOB, as well as dose-specific information, such as expiration date and time given).

As the pharmacy team was the only unblinded staff within the ENSEMBLE study, the trailer had a designated secure room to process orders and prepare doses. That secured room ensured the proper blindness during the study, as well as minimized the traffic for all investigational product preparations. All investigational products were prepared in a biosafety level II cabinet given the nature of the study. The consistency of medication preparation in a biosafety cabinet ensured the quality of medication for the study, and also maximized the safety of the personnel involved in the preparation steps. After a participant-specific dose was prepared, the pharmacist would place the prepared syringe with its administration sheet in a clear bag labelled with the participant's identification information (ie name, age, gender and medical record number) and leave it in a clear tray outside the pharmacy area for medical assistants to pick up. Effective communication about dose preparation and readiness between pharmacists and medical assistants was carried out via a handheld transceiver. At the end of each day, the paperwork from the trailer and clinic settings were combined and stored in a locked space within the IDS pharmacy area.

For a clinical setting that used trailer units, it was important for vaccine preparation and administration to be performed within the same trailer unit to minimize the variation caused by transportation or possible exposure of the vaccine to the environment. The unit temperature was monitored and controlled carefully by the university's engineering department to ensure that temperatures in all trailer units were maintained consistently.

## 3 | WHAT IS NEW

Using trailer units was unique to this study location; this strategy offered the research team a broader coverage area, which was especially useful in reaching underserved communities with transportation limitations. This method could also increase enrolment within a given period of time even with social distancing compliance.

During this pandemic, strictly following social distancing rules is considered one of the key factors responsible for slowing down potential disease transmission. As a result, a clinic may need a larger physical area than usual to provide services in locations with limited public resources, such as health care or transportation. The trailer settings allowed us to maintain extended business hours and keep up with study demands. In the mobile unit, the first trailer was dedicated to participant registration and consent; after consenting, participants were brought to the second trailer for a physical examination, while the third trailer was dedicated to phlebotomy work and sterile preparation for pharmacy operations and investigational

vaccine administration. The three-trailer clinic setting ensured the proper compliance of social distancing guidelines as per FDA and Center for Disease and Prevention (CDC) recommendations. In addition, as participants were actively moving to a different trailer as they proceeded to the next step of the study, we observed that the move of participants improved their clinic visit experience, as participants felt the progress within the study visit. In addition to the physical space expansion, these trailers could be re-located and serve as satellite study visit centres while reaching out to minority communities. As some of the members in minority communities experienced transportation issues, limiting their ability to visit a hospital or clinic, the flexible location of trailer clinic increased the participation in those minority communities, benefiting the entire study by increasing its diversity.

Traditionally, an investigational drug study may take months or even years to enroll a sufficient number of participants into the study; however, given the unique time frame during this pandemic, all parties involved emphasized the importance of enrolling as many participants (up to 40,000), as quickly as possible. The compact trailer spaces and minimal distance from the pharmacy to the dose administration site brought benefits to the study, such as increased effectiveness of communication and reduced transportation time of the prepared vaccine. These factors further contributed to faster turn-over time in the trailer settings compared to clinic settings. In a clinic setting, the average participant turn-over time was between 2 and 3 h, depending on the availability of personnel and spaces (eg limited examination rooms). In a trailer, which is more compact, the study team was able to improve the turn-around time to 1.25–1.5 h per participant. The faster turn-over rate resulted in a higher number of participants processed within the given time period, allowing to enroll more participants on each day and reaching the study enrolment goal sooner than expected. Although the use of trailer units was initiated 2 months later than the clinic setting in this study, the mobile study team was able to match the enrolment number of participants between the clinic setting and trailer setting. Overall, the addition of flexible trailer units expanded clinic capacity and service location coverage, while maintaining compliance with social distancing rules during the current pandemic.

As research teams and manufacturers are racing to develop and produce potential vaccines, both study teams and pharmacies require flexibility, especially since the final protocols and processes have not been fully established by the time these studies are being conducted. Although FDA reviews the full safety and efficacy profiles prior to approving human clinical trials, given the short duration of study time and the fast-track process unique to the COVID-19 vaccine trials, safety information is continually updated. When any safety concerns are reported to the FDA, the study is typically paused while an investigation and evaluation take place, and the manufacturer may be required to modify the protocol based on the FDA recommendations.

When such modifications occur, the entire study team, including the IDS pharmacy, is notified and possibly re-trained for compliance with the updated protocol. Being able to stay on top of these modifications plays a key role in ensuring participant study validity.

## 4 | CONCLUSION

As an investigation drug pharmacy, it is important to develop an easy-to-follow workflow for each study in order to guide daily activities, minimize personnel error and ensure the scientific quality of the study. The University of Chicago Medicine investigational drug services pharmacy developed a workflow for the ENSEMBLE Phase III trial that could contribute to other sites carrying out similar trials during the COVID-19 vaccine development period. The method of transitioning clinic into trailer settings or even mobile units benefited the study in multiple ways. These units were considered as an extension to the clinic and served as individual sites that expanded the service area and allowed increased participant enrolment within a limited time period. The more compact design helped the study team to increase the turn-over rate of each participant, leading to higher efficiency of the study workflow. We hope to share this trailer clinic design, or even to transition these clinic settings into mobile units in future to maximize the flexibility of our service while maintaining the protocol compliance.

## CONFLICT OF INTEREST

No conflicts of interest have been declared.

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## REFERENCES

1. Graham BS. Rapid COVID-19 vaccine development. *Science*. 2020;368(6494):945–946.
2. Jeyanathan M, Afkhami S, Smaill F, Miller MS, Lichty BD, Xing Z. Immunological considerations for COVID-19 vaccine strategies. *Nat Rev Immunol*. 2020;20:615–632.
3. Corey L, Mascola JR, Fauci AS, Collins FS. A strategic approach to COVID-19 vaccine R&D. *Science*. 2020;368(6494):948–950.
4. Kaur SP, Gupta V. COVID-19 vaccine: a comprehensive status report. *Virus Res*. 2020;288:198114.

**How to cite this article:** Li N. Participation in ENSEMBLE phase III multicenter clinical trial of Ad26.CoV2.S, a COVID-19 vaccine: An investigational drug services perspective. *J Clin Pharm Ther*. 2022;47:360–362. <https://doi.org/10.1111/jcpt.13476>