Cohort Event Monitoring (CEM) for Safety Signal Detection, after Vaccination with COVID-19 Vaccines and Post Market Monitoring in Nigeria

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Final Technical Report

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Collaborating Institutions

The National Agency for Food and Drug Administration and Control (NAFDAC)

Centers for Disease Control and Prevention (CDC)

Center for International Health, Education, and Biosecurity (CIHEB) at the University of Maryland, Baltimore (UMB)

The Task Force for Global Health

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Executive Summary

The World Health Organization (WHO) Cohort Event Monitoring (CEM) guidelines provide a valuable framework for monitoring the safety and effectiveness of pharmaceuticals and vaccines after they have been approved and are in use by the general population. CEM is a post-marketing surveillance method aimed at detecting, assessing, and understanding adverse events (AEs) associated with the use of medicines and vaccines in real-world settings. It involves monitoring a cohort of patients who have been prescribed a specific medication or vaccine over an extended period, typically years. Cohort Event Monitoring (CEM) seeks to fill the safety data gap between phase 3 clinical trials and routine passive surveillance (1).

This evaluation adopted the CEM methodologies as proposed by the WHO to evaluate adverse events following COVID-19 vaccination in Nigeria. This report describes the adverse events observed in cohorts of individuals who received either AstraZeneca or Pfizer vaccines (CEM Phase 1), and AstraZeneca, Johnson and Johnson or Pfizer vaccines (CEM Phase 2), followed up for 3-6 months and 1 year respectively in Nigeria. This evaluation provides a quick and easy way to actively follow up on adverse events in persons exposed to the COVID-19 vaccines and the data generated will provide reassurance of safety for regulators, immunization programs, and the public. With funding support from CDC and government leadership through NAFDAC, UMB implemented the two CEM evaluations under the NAIIS project with strong collaboration with the Taskforce for Global Health and members of the academic community in Nigeria.

Background

At the end of 2019, a novel coronavirus started as an emerging pathogen for humans and resulted in a pandemic. The source of the pandemic was traced back to a wild live animal market in the Huanan Seafood Wholesale market in Wuhan, a city in the Hubei province of China. From there, the virus spread across the globe, with cases being reported from every continent. SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), the virus causing coronavirus disease 2019 (COVID-19), is a positive-stranded RNA virus, like other coronaviruses. On March 11, 2020, the WHO declared COVID-19 a pandemic as the number of infected countries grew.

The introduction of COVID-19 Vaccines is a key public health measure taken to mitigate the negative effects of COVID-19 at both individual and community or population levels. Vaccination as a most effective measure to reduce the risk of severe COVID-19 disease prevents not only deaths but also reduces hospital admissions, which subsequently decreases the burden on healthcare personnel, supplies, and facilities, and reduces the impact of COVID-19 on other diseases.

Nigeria confirmed the first novel coronavirus disease 2019 (COVID-19) case in February 2020. The COVID-19 vaccination program in Nigeria began in March 2021 and is the largest vaccination program held in Nigeria.

About 4 million doses of the first vaccine, AstraZeneca/Oxford, arrived in the country on March 2, 2021, through the COVID-19 Vaccine Global Access (COVAX) facility, in partnership with Coalition for Epidemic Preparedness Innovations (CEPI), Global Alliance for Vaccines and Immunizations (GAVI), United Nations Children's Fund (UNICEF), and WHO.

Immediately after the arrival of the vaccine, vaccination began with the frontline health workers as they are one of the most prioritized groups to receive the COVID-19 vaccine. Since the arrival of the first wave of vaccines, the country has received more than 67 million doses of COVID-19 vaccines, out of which 31.1 million people have been fully vaccinated. Currently, six (6) additional vaccines have been approved for use in Nigeria. These include Moderna, Pfizer/BioNTech, Gamaleya, Janssen (Johnson & Johnson), and Sinopharm (Beijing).

These COVID-19 vaccines were developed at unprecedented speed to prevent severe SARS-CoV-2 infection and were conditionally authorized by regulators in December 2020. The large-scale vaccination campaigns for these vaccines undeniably raised the importance of post-authorization evaluations not only through spontaneous reporting but also by cohort event monitoring to obtain more in-depth vaccine safety information, rapidly after launch.

Vaccine safety is paramount, with regular assessments and post-approval clinical studies to report on its safety and effectiveness. The WHO recommended designing and implementing prospective cohort studies. Such studies can follow up on vaccinated individuals regularly and record the adverse events.

Thus, systematic vaccine safety surveillance and dissemination of key findings is critical for ensuring the safety of vaccines and mobilizing public trust through informed processes. In any country, once a plan for immunization with COVID-19 vaccines is set up, pharmacovigilance efforts should start simultaneously, as conceptualized in the WHO Smart Safety Surveillance (3S) principles. Furthermore, specific COVID-19 vaccine safety surveillance should be implemented as described in the WHO safety surveillance manual.

1.0 Phase 1 CEM

The Phase 1 CEM sought to monitor the safety of enrolled individuals who have received authorized COVID-19 vaccines in Nigeria (AstraZeneca and Moderna) across six geopolitical zones within 3 months of each vaccine dose. The specific objectives were to:

1. Characterize adverse events following immunization (AEFI) among persons receiving COVID-19 vaccines, including medically attended events (MAEs), serious adverse events (SAEs), and adverse events of special interest (AESIs).
2. Estimate the incidence of SAEs in all enrolled vaccinated participants after each COVID-19 vaccine dose, or after the combined two doses, by COVID-19 vaccine brand.
3. Estimate the incidence of AESIs in all enrolled vaccinated participants after each COVID-19 vaccine dose or after the combined two doses, by COVID-19 vaccine brand.
4. Estimate the incidence of reactogenicity within seven days after each COVID-19 vaccine dose, by COVID-19 vaccine brand.
5. Estimate the incidence of COVID-19 for the possibility of vaccine-associated enhanced disease (VAED).

CEM Phase 1 Design and Methodology

1.1 Study Area

The CEM Phase I evaluation was conducted in six states - the Federal Capital Territory (FCT), Bauchi, Benin, Edo, Enugu, and Kaduna. Participants were recruited from six high-volume tertiary health facilities (‘hubs) and at least five associated health facilities (spokes) in the six geopolitical zones of the country used as vaccination centers for administration of COVID-19 vaccines. Enrollment, follow-up and outreach took place at the hubs, whereas only enrollment of participants was conducted at the spokes. Study sites were selected based on the availability of

sufficient and trained human resources, access by target population, geopolitical location, size of population covered, vaccination coverage, and access to a computer for data collection at the site level.

Table 1: Surveillance sites for Phase 1 CEM with principal investigators/Supervisors

Geopolitical Zone	State	Study Site	Investigators/ Study Coordinators/ Supervisors
NW	Kaduna	Ahmadu Bello University Teaching Hospital, Zaria	Prof. Ibrahim Abdu-Aguye
			Pharm. Foluke Garnett
NC	FCT	University of Abuja Teaching Hospital, Gwagwalada	Dr. Peter Bassi
			Dr. Ramsey Yalman
SW	Lagos	Lagos University Teaching Hospital, Lagos	Prof. Ibrahim Oreagba
			Dr. Adewunmi Debo
SE	Enugu	University of Nigeria Teaching Hospital, Enugu	Prof. Becky Tagbo
			Pharm. Adeline Osakwe
SS	Edo	University of Benin Teaching Hospital, Benin	Dr. Abimbola Opadeyi
			Pharm. Muktar Andullahi Babatunde
NE	Bauchi	Abubakar Tafawa Balewa Teaching Hospital, Bauchi	Dr. Ibrahim Maigari
			Dr. Salisu Idris

1.2 Sampling Methods

1.2.1 Sample size for overall cohort

For Phase I of the CEM evaluation, a total of 12,317 participants across the six participating tertiary hospitals were enrolled and followed-up between September 9, 2021, and March 31, 2022. In the sample size calculation, 12,000 participants were estimated to exclude occurrences with a rate of one per 3,333 with 95% confidence if an event was not detected (1).

1.3 Recruitment, Eligibility Criteria, and Consent Procedures

1.3.1 Recruitment

Participants were recruited among individuals vaccinated at selected sites that participated in this CEM evaluation. Participation was strictly voluntary. The CEM enrollment and follow-up process was done by two categories of field staff: the data entrants and the follow-up clinicians. The data entrants entered the participants' data and then the follow-up clinicians called the participants on Day 0, Day 3, and Day 7, checking for any AEFIs that may have occurred. The implementation design followed a series of processes, such as advertisement and recruitment of

research assistants, advocacy campaign by the study principal officers, and training of the recruited research assistants. The role of data entrants was to collect and enter participants' data (electronically, with the use of a tablet), complete the participants' baseline information (demographic and medical) and contact information (of participant and participant's next of kin), and record details of vaccination. A unique participant number was generated for each participant who gave consent to be followed up. The follow-up clinicians contacted the participants thereafter via phone calls on Day 0, Day 3, and Day 7, respectively, after their vaccinations and once weekly thereafter. This was done to record any occurrence of AEFIs. Similarly, the participants were monitored after they took their second dose of the vaccine.

1.3.2 Eligibility/Inclusion Criteria

- Individuals who had received the COVID-19 vaccine and were 18 years and above.
- Ability and willingness to give informed consent in English, Pidgin English, Yoruba, Hausa, or Igbo.
- First dose of a COVID-19 vaccine already received at a vaccination centre participating in the surveillance activity.
- Individuals with a history of hypersensitive reactions/allergy to vaccines, immunosuppression, pregnant/breastfeeding women.

1.3.3 Exclusion Criteria

- Participants already vaccinated with any other COVID-19 vaccine before enrollment, irrespective of the brand.
- Participants unable to comply with study procedures (e.g., illiterate, cognitively impaired, etc.)
- Individuals with current or history of substance addiction.
- Individuals who refused to consent at enrollment or those who withdrew consent at any time following enrollment.

1.3.4 Withdrawal and loss to follow-up

- A participant had the right to withdraw from the surveillance at any time and for any reason.
- A participant was considered lost to follow-up after five unsuccessful attempts within one week to contact the participant by phone, followed by five unsuccessful attempts within a week to contact participants' next of kin. All contact attempts were documented.
- Attempts were made to determine the underlying reason(s) for the withdrawal and, where possible, the primary underlying reason was recorded.

- Withdrawn participants and participants lost to follow-up were not replaced after the enrollment period had ended.
- For a participant who decided to withdraw, data collected up until time of withdrawal were included in the analysis except if the participant requested that the data should not be used.

1.4 Ethical Approval

Participating sites submitted National Health Research Ethics Committee (NHREC) approval to the site-specific Institutional Ethics Committee(s)/Institutional Review Board(s) (IRB) for documentation, following local regulations and compliance with any national ethics committee requirements. The protocol was also submitted to the United States Centers for Disease Control and Prevention (CDC) for approval of a determination of non-human subjects' research, as well as to the University of Maryland, Baltimore (UMB) IRB for approval.

1.5 Data Collection and Management

Data were collected at the time of enrollment and during follow-up by data entrants who were part of the study evaluation staff. Data collection at enrollment and vaccination was done on tablets using an electronic data collection tool – census and survey processing system (CSPro, version 7.4) (2). Participation in the evaluation was voluntary with no form of incentive, compensation, or payment from the organization. Data were collected during the three-month follow-up period by telephone interviews. Responses from participants were documented in the electronic data collection tool in real time. Enrollment activities took place within a month across all 36 study sites in the six states.

Participants aged 18 years and above who consented to take part in the study were enrolled and followed up for three months if they only received one dose of vaccine and for six months for those who received the first and second dose of AstraZeneca or Moderna vaccine. Completed questionnaires and hospital/laboratory data were stored on the data collection devices and sent daily directly to the central server through a secured connection. Data transmission was monitored centrally, and support was provided to the data collection teams for timely synchronization. Reports with an adverse event were routed to the country's VigiFlow system using an E2B file, while other reports were exported as a CSV file for further analysis. 1.6 Definitions and Classifications of Events

1.6.1 Reactogenicity

Reactogenicity was categorized as either local or systemic reactogenicity. Local reactogenicity was defined as the presence of pain, redness, warmth, swelling, hardening/ induration, hematoma, or itching at or near the injection site. Systemic reactogenicity was characterized as

the presence of fever, chills, headache, nausea, muscle or joint discomfort, or feeling unwell. Both categories of reactogenicity were recorded within the first eight days of the first dose at Day 3 and Day 7 post-vaccination, respectively, where the first day was recorded as Day 0. Participants were retrospectively asked about any new medical events including systemic symptoms in the three days prior to enrollment (excluding the day of enrollment).

1.6.2 Medically Attended Events

Medically Attended Events (MAES) were defined as adverse reactions that led to seeking medical care from a health practitioner or pharmacist, or health facility during any period of follow-up.

1.6.3 Serious Adverse Events

Events that resulted in death, were life-threatening, necessitated inpatient hospitalization or prolongation of an existing hospitalization, caused persistent or significant disability/ incapacity, or constituted congenital birth defects were referred to as serious adverse events (SAEs). SAEs associated with hospitalization were reported by the participant or next of kin while those resulting in death were reported by the next of kin.

1.6.4 Identification of MAEs and SAEs

The diagnoses reported by the participants during follow-up were coded using Medical Dictionary for Regulatory Activities (MedDRA) (3) by data managers. MAEs, and SAEs were identified by the MedDRA coding trained data managers. Reported MAE, or SAE were followed up for investigation using the already documented in-country approach for investigation of serious AEFIs. The State Epidemiologist and Disease Surveillance and Notification Officers (DSNOs) for that State where the cases occurred was involved in the investigation of the cases. All necessary medical reports related to each case were obtained for appropriate documentation by data managers.

1.7 Data Analysis

Participation rate over time was described, and demographic characteristics at enrollment were summarized using frequencies and percentages. Analysis of reactogenicity was conducted on participants with follow-up information between zero and seven days of receiving a vaccine, while MAEs and SAEs included all participants with at least one follow-up. Completion of the follow-up interviews by participants with no disclosure of an event was reported as the absence of an event. Missing values were not inputed. Frequencies and percentages of MAEs and SAEs were provided for all reported cases. Length of time from first vaccination (reported in weeks) was considered in calculations of the likelihood of occurrence of identified SAEs among participants. Determination of diagnoses was carried out using Preferred Terms (PTs) assigned

by MedDRA while 95% confidence intervals for proportions were determined precisely. The frequency of participants reporting reactogenicity, MAEs, and SAEs were assessed and reported as percentages and grouped by age group, sex, vaccine brand, and risk group. Furthermore, incidence of MAEs and SAEs was calculated for the overall population and by age group, sex, vaccine brand, risk group, and pregnancy using the number of person-years contributed by each participant with the associated confidence interval.

Person-years of follow-up contributed by the cohort were accumulated for each client from the date of first vaccination (enrollment date) until the date of last contact or first diagnosis of any MAEs or SAEs. The 95% confidence intervals of the incidence rate were calculated using an exact method.

A multivariate Poisson regression was used to estimate the incidence rate ratios of reactogenicity, MAEs, and SAEs reporting by age group, sex, vaccine brand, and risk group with 95% confidence intervals. The incidence of COVID-19 disease ascertained by laboratory testing, diagnosis by a health professional, admission to a hospital or intensive care unit, or related death, was calculated by dose classification and by the interval between doses. The appearance of COVID-19 symptoms within one-to-two days after vaccination was a basis for exclusion of participants from the study.

1.8 Data Management

A data management plan (DMP) describing all related data activities and processes and outlining critical steps to ensure data collection and validation, including roles and responsibilities of staff, was developed prior to the onset of data collection. The data collection staff were responsible for the entry of the data into the tablets. The evaluation staff were responsible for ensuring completion of the ICF and collection of other pertinent information such as participants demographic information, enrollment date, details about the vaccine, relevant information from interviews and medical charts, where applicable, and any data obtained in the event of additional follow-up after initial non-response. Data collected were stored on UMB in-county servers with a backup database restored at the National Agency for Food and Drug Administration (NAFDAC) office.

1.8.1 Data Security

Participants were assigned a unique identification number for identifying their responses. The link to participants' personal information was maintained by authorized members of the evaluation team. All electronic databases were encrypted, and password protected to ensure confidentiality. Access to electronic data was restricted to authorized evaluation staff, such as the data managers and investigators. For events that required prompt identification and

response by EPI and NAFDAC, patient identification details were made available to the relevant persons via Nextcloud, a client-server software for creating and using file hosting services which supports all technical safeguard requirements and is in full compliance with the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

1.8.2 Data Transfer

Data uploaded by the data entrants were transmitted to the central evaluation server over the internet using secured https protocol. Data was only accessed for follow-up over the internet using secure https protocol. Hence, data was handled with high confidentiality and security checks.

1.9 Key Findings

- Of the 12,317 consenting participants, 6,990 (56.7%) received AstraZeneca vaccine while 5,327 (43.3%) received Moderna vaccine.
- 11,911 (96.7%) enrolled participants were reached for follow-up of which 7,869 (66.1%) received second dose of vaccine (AstraZeneca 49.3%, Moderna 50.5%).
- 3.3% of vaccinees were lost to follow-up.
- A total of 10,618 (89.1%) participants completed the follow-up schedule among 11,911 that were followed up.
- 72.0% (2,912/4,042) of those who received only the first dose of a vaccine completed the three-month follow-up, while 97.9% (7,706/7,869) had complete follow-up among those who received first and second doses of a vaccine.
- Within day 0 – 7 post- first or second dose vaccination 56.3% & 36.5% of followed-up participants experienced at least one local reactogenicity symptom and 41.1% & 30.6% reported systemic symptoms respectively.
- Pain at the injection site was the highest reported local reactogenicity; 95.8% & 98.0% for AstraZeneca and 97.2% & 98.5% for Moderna vaccinees after first and second vaccine doses respectively.
- Fever was the most commonly reported systematic reactogenicity; 57.4% & 47.7% for AstraZeneca and 52.9% & 69.6% for Moderna vaccinees after first and second vaccine doses respectively.
- Out of 11,911 participants that were followed up, 6.6% (786) reported that they sought medical care (MAEs) at least once post vaccination.
- Of the 11,911 participants, 75 (0.6%) were hospitalized (SAEs) – 32 (0.6%) among those who received Moderna and 43 (0.6%) for AstraZeneca.
- Participants reporting positive SARS-CoV-2 result were 0.2% (11) among AstraZeneca and 0.3% (14) Moderna vaccinees respectively.

2.0 Phase 2 CEM

Phase 2 CEM aimed to monitor and evaluate the safety of COVID-19 vaccines in enrolled adults over the age of 18, across Nigeria's six geopolitical zones, for the purpose of safety signal detection and management for a 12-month period following first vaccine dose. Specific objectives were:

1. Estimate the incidence of serious adverse events (SAEs) in all enrolled vaccinated participants after each COVID-19 vaccine dose, by COVID-19 vaccine brand.

2. To estimate the incidence of adverse events of special interest (AESIs) that result in hospitalization in all vaccinated individuals enrolled after each dose of COVID-19 vaccine, by vaccine brand.

3. To estimate the incidence of reactogenicity within 7 days of each vaccine dose of the COVID-19 vaccine by vaccine brand.

4. To measure the association between exposure to COVID-19 vaccine by vaccine brand and detected serious adverse events.

CEM Phase II Design and Methodology

2.1 Study Design

Active COVID-19 vaccine safety surveillance through an observational prospective single-arm cohort design was conducted. Participants were actively screened for the occurrence of adverse events, including medically attended events, at pre-specified intervals for 1 year after their first COVID-19 vaccine dose. All participants who screened positive for a medically attended event at any screening contact were interviewed by trained follow-up personnel to collect additional information with the comprehensive CEM questionnaire. For two-dose vaccines, even if a participant did not receive the second dose, the full 1-year data collection period following the first dose was completed.

2.2 Study Area

Participants were recruited from six tertiary (Hubs) and four associated lower-level healthcare facilities (spokes) across Nigeria's six geopolitical zones, with each tertiary facility used as a vaccination center for the administration of COVID-19 vaccines to individuals. Participant enrollment, follow-up, and outreaches for COVID-19 vaccination were conducted at the hubs, while only enrollment of participants was conducted at the spokes.

Sites were selected based on the availability of sufficient and trained human resources, access by target population, geopolitical location, size of population covered, vaccination coverage, and access to computers for data collection at the site level.

Table 2: Surveillance sites for Phase 2 CEM with principal investigators

Geopolitical Zone	State	Study Site	Principal Investigators
NC	FCT	University of Abuja Teaching Hospital, Gwagwalada	Dr. Ramsey Yalma
SW	Lagos	Lagos University Teaching Hospital, Lagos	Prof. Ibrahim Oreagba
			Dr. Adewunmi Debo
SS	Edo	University of Benin Teaching Hospital, Benin	Dr. Abimbola Opadeyi
SE	Enugu	University of Nigeria Teaching Hospital, Enugu	Prof. Becky Tagbo
NW	Kano	Aminu Kano Teaching Hospital, Kano	Dr. Usman Bashir
NE	Bauchi	Abubakar Tafawa Balewa University Teaching Hospital, Bauchi	Dr. Ibrahim Mahmood Maigari

2.3 Sampling Methods

A sample size of 20,000 participants was calculated to rule out events with a frequency of 1 per 6,666 with 95% confidence if no event is detected (1). To account for the loss, an anticipated 10% loss to follow-up with an additional 2,222 individuals was proposed to make the total of 22,222 participants. Altogether, about 3,400 participants from each of the 6 participating tertiary hospitals were to be enrolled for follow-up.

A total of 17,474 participants were eventually enrolled in the study and followed up between June 20, 2022, and August 31, 2023, across all the participating sites.

2.4 Eligibility Criteria, Recruitment, and Consent Procedures

2.4.1 The eligibility criteria, recruitment and consent procedures remained the same as the Phase 1 study.

2.4.2 Recruitment and Informed Consent

Participants were identified and enrolled using active enrolment strategies including mobilization through advocacy and sensitization at each of the participating vaccination sites. Enrollment activities took place for three months across all 36 study sites in the six states. Informed consent was received from each participant before they were finally enrolled in the study. The vaccination sites were public healthcare facilities used during CEM phase 1. The CEM team provided participants with additional information including who to contact with questions at any time during the evaluation, follow-up contact schedule, follow-up with their next of kin/alternate contact if necessary and answer any questions they may have. If participants received a second COVID-19 vaccine dose during the follow-up period, details of the second vaccination or any additional doses were also collected.

2.4.3 Withdrawal and loss to Follow-up

- A participant had the right to withdraw from the surveillance program at any time and for any reason.
- A participant was considered lost to follow-up after three consecutive missed contacts followed by three unsuccessful attempts to reach them and two unsuccessful attempts within the same period to contact the participant's next of kin. The contact attempts were documented.
- Withdrawn and lost to follow-up participants were not replaced after the enrolment period had ended.
- For a participant who decided to withdraw, data collected up until the time of withdrawal were included in the analysis unless the participant explicitly requested otherwise.

2.4 Ethical Approval

The protocol was submitted to the National Health Research Ethics Committee (NHREC), UMB, and CDC institutional review boards (IRB) for approval following local regulations and compliance with national ethics committee requirements.

2.5 Data Collection and Management

Data were collected at the time of enrollment and during follow-up by data entrants who were part of the study evaluation staff. Data collection at enrollment and vaccination was done using CSPro (2). Participants were referred for a comprehensive interview by the FPC if they reported to have sought medical care or been hospitalized. The comprehensive interview collected

detailed information on reported AESIs, SAEs, and MAEs. Reports with an adverse event were routed to the adverse drug reaction (ADR) database such as the Vigilance Hub using an E2B R3 XML file or JSON format while other reports were exported as a CSV file for further analysis as done in phase 1.

Participation in the evaluation was voluntary with no form of incentive, compensation, or payment from the organization. Data were collected during the one-year follow-up period by telephone interviews. Responses from participants were documented in the electronic data collection tool in real-time. Initial follow-up was done for participants on days 3 & 8 (following administration of doses 1 & 2) to check for anaphylaxis and reactogenicity, and medically attended events (MAEs); and monthly contact up to month 3 (weeks 4, 8 & 12) after the first dose to check for AESIs, MAEs, and pregnancy. Subsequently, quarterly follow-ups were conducted for one year after the first dose. Completed questionnaires and hospital/laboratory data were stored on the data collection devices and sent directly to the central server through a secured connection. Data transmission was monitored centrally, and support was provided to the data collection teams for timely synchronization. Reports of adverse events were routed to the country's VigiFlow system using an E2B file, while other reports were exported as a CSV file for further analysis.

2.7 Key Findings

- Of the 17,474 consenting participants enrolled into this study, 12,253 (70.1%) received Johnson & Johnson, 5,057 (28.9%) received Pfizer and 164 (0.9%) received AstraZeneca vaccines respectively.
- 17, 031 (97.5%) enrolled participants were reached for follow-up.
- 16,584 (97.4%) of followed-up participants completed 1-year follow-up, with a loss to follow-up rate of 2.3%.
- 39 (0.2%) participants reported anaphylaxis within 3 – 8 days of receiving first vaccine dose, while 1 (0.1%) participant reported anaphylaxis within 3 – 8 days of receiving second dose of vaccine.
- Commonest anaphylactic reactions reported were altered consciousness, difficulty with breathing, dyspnea, rash, and tachycardia.
- 7,052 (41.2%) of followed-up participants reported reactogenicity within 3 – 8 days of receiving the first vaccine dose.
- Of 808 participants who received the second vaccine dose, 248 (30.7%) reported reactogenicity with 3 – 8 days of receiving the second vaccine dose.
- Across all vaccine brands, systemic reactogenicity was more common than local reactogenicity (AstraZeneca 76.6% cf 46.7%; Pfizer 61.2% cf 59.3%; Johnson & Johnson 78.3% cf 40.5%).

- Across all vaccine brands, there were slightly higher proportions of reported reactogenicity among female participants, those who were diagnosed with a new medical condition 90 days pre-vaccination, and those who took any medication the last 90 days pre-vaccination.
- Commonest local reactions reported were injection site reactions, joint pain, and limb discomfort, while the commonest systemic reactions reported were pyrexia, headaches, fatigue, and myalgia.
- Of the 17,031 participants reached for follow-up, 280 (1.6%) reported MAEs, 5 (3.2%) among Astra Zeneca vaccinees, 92 (1.9%) among Pfizer vaccinees, and 183 (1.5%) among Johnson & Johnson vaccinees.
- Malaria symptoms, fever, high blood pressure, body aches, headaches, and asthma were the most reported MAEs.
- 18 (0.1%) participants reported SAEs (11 (0.1%) among Johnson & Johnson, and 7 (0.1%) among Pfizer vaccinees)
- 5 participants were confirmed dead by their next of kin at the end of the study period. Reported causes of death were suicide, indoor accident, and car accident.
- 5 participants reported AESIs (4 cases of anaphylaxis among Johnson & Johnson vaccine recipients, and 1 case of convulsion among Pfizer vaccine recipients).

3.0 Conclusions

- No vaccine related mortality was recorded during the follow-up period for CEM Phases 1 and 2
- The AstraZeneca, Johnson and Johnson, Pfizer, and Moderna COVID-19 vaccines are relatively safe as the adverse events recorded were not severe among most of the participants.
- The findings of these evaluations provide further assurance of the safety profile of these vaccines and will inform public health messaging as well as guide post-market licensure of the vaccines.
- Strong collaboration with government agency (NAFDAC) and academics has fostered capacity transfer for future evaluations.

4.0 Recommendations

- The findings of these evaluations should be used to strengthen vaccine campaign messaging and design of vaccine programs in the country.
- Special attention should be paid to developing messages to encourage the completion of vaccine doses.
- As much as possible, single-dose vaccines should be encouraged to enhance vaccine completion rates.

- Surveillance systems to facilitate longitudinal follow-up of COVID-19 vaccinees are recommended to continue to enhance public trust and contribute to global learning on COVID-19 vaccines.

5.0 Challenges and Mitigation Steps

Challenges	Mitigation Steps
Low vaccination uptake leading to low enrolment rate	We leveraged on outreach and mobile vaccination teams to reach more enrolees
Industrial action by vaccination mobile teams in some states	Logistic support was provided for mobile outreach teams as an incentive to work

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Appendices

Appendix 1: List of Contributors

Teams	Capacity	Organization	Name
Surveillance team	Principal Investigators	National Agency for Food and Drug Administration and Control	Prof. Moji Adeyeye
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		University of Abuja Teaching Hospital	Dr. Peter Bassi
		US CDC	Dr. Omotayo Bolu
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		University of Abuja Teaching Hospital	Dr. Peter Bassi
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		University of Nigeria Teaching Hospital, Enugu	Prof. Becky Tagbo
		University of Benin Teaching Hospital	Dr. Abimbola Opadeyi
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	Surveillance coordinator	University of Nigeria Teaching Hospital	Pharm Adeline Osakwe
		University of Benin Teaching Hospital	Pharm. Muktar Andullahi Babatunde
		ABUTH Zaria	Prof. Ibrahim Abdu-Aguye
		UATH Abuja, FCT	Dr. Ramsey Yalman
		Lagos University Teaching Hospital	Dr. Adewunmi Debo
		Abubakar Tafawa Balewa Teaching Hospital, Bauchi (ATBUTH), Bauchi State	Dr. Salisu Idris
Other Contributors		University of Maryland, Baltimore	Dr. Oluwasanmi Adedokun Dr. Baffa Ibrahim Oluwafemi Alo Gladys Antonza Abisinuola Lawal Adekemi Adepoju Favour Makava Musa Saiki Sulaiman Abaniwonda Frank Encisco Sandra Ozordi Samuel Indyer Samuel Nwafor
		US CDC	Adeyelu Asekun Scholastica Obianyor Asuquo Akpan
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Data owner		NAFDAC, Nigeria	
Sponsor		Federal Government of Nigeria/US CDC	

Appendix 2: List of Field Staff

S/N	Designation	Name
1	Follow-Up Personnel	Olufemi Olajumoke
2	Follow-Up Personnel	Edem Magdalene Hanson
3	Follow-Up Personnel	Sani Ibrahim
4	Follow-Up Personnel	Elizabeth Ogah
5	Follow-Up Personnel	Christopher Asheama Rachael
6	Follow-Up Personnel	Halimat Onize Anate
7	Follow-Up Personnel	Abdulrahman Hamdalat Modupe
8	Follow-Up Personnel	David Akinola Junior
9	Follow-Up Personnel	Abaniwonnda Azeezah Osaro Jennifer
10	Follow-Up Personnel	Nwafor Godsgift Adaku
11	Follow-Up Personnel	Ojo Lola Elizabeth
12	Follow-Up Personnel	Hadiza Abashe
13	Follow-Up Personnel	Kyangma Eunice Kasham
14	Follow-Up Personnel	Ibeh Chioma Lilian
15	Follow-Up Personnel	Reuben Chikadibia Prince
16	Follow-Up Personnel	Abdullahi Jumai Adama
17	Follow-Up Personnel	Okudili Anene Onwughalu
18	Follow-Up Personnel	Uwakmfon Aniefiok Ekerette
19	Follow-Up Personnel	Temple A. Oparaocha
20	Follow-Up Personnel	Ezra Babatunde Oluwaseyi
21	Follow-Up Personnel	Elemuwa Adaeze
22	Follow-Up Personnel	Nnabuchi Chidimma Ezekwe
23	Follow-Up Personnel	Awotunde Favour Anuoluwapo
24	Follow-Up Personnel	Jummai Abdullahi
25	Follow-Up Personnel	Anikwe Chinedu
26	Follow-Up Personnel	Sani Rukayat Ahmed
27	Follow-Up Personnel	Toye Timilehin Eyitayo

28	Follow-Up Personnel	Auwal Abubakar Doguwa
29	Follow-Up Personnel	Samuel Peace Chizurumoke
30	Follow-Up Personnel	Godwin Odido
31	Follow-Up Personnel	Vandu Alfred Emmanuel
32	Follow-Up Personnel	Igwe Philip Chinonso
33	Follow-Up Personnel	Adegboye Rachael Oluwatosin
34	Follow-Up Personnel	Bello Tosin Basirat
35	Follow-Up Personnel	Oparanozie Barbara Marachi
36	Follow-Up Personnel	Momoh Ojima Jerry
37	Follow-Up Personnel	Wichendu Yvonne
	ENUGU	
38	Data Entrant	Nwafor Amarachi Juliet
39	Data Entrant	Chidi Favour Adaeze
40	Data Entrant	Onuko Ikechukwu
41	Data Entrant	Henshaw Victoria Utibe
42	Data Entrant	Enyinnah Felicity Chimdinma
	LAGOS	
43	Data Entrant	Essien, Happiness
44	Data Entrant	Dan-Ojile Favour
45	Data Entrant	Ogunleye Adefunke Busola
46	Data Entrant	Asiegbu Chioma Chika
47	Data Entrant	Glory Obike
	EDO	
48	Data Entrant	Osade Mwingie Blessing
49	Data Entrant	Erhunmwunse Eki Blessing
50	Data Entrant	Osemwengie Abienwense B
51	Data Entrant	Ogene Justice Ogie
52	Data Entrant	Oni Ibukunoluwa Christabel
	BAUCHI	

53	Data Entrants	Jacob Peter Akau
54	Data Entrants	Esther Samuel
55	Data Entrants	Odugbo Abdulkareem
56	Data Entrants	Bature Weng Ayuba
57	Data Entrants	Adebayo Azeez Arisekola
58	Data Entrants	Abdulaziz.T. Saidu
	FCT	
59	Data Entrants	Henry E. Samuel
60	Data Entrants	Makinde M. Simeon
61	Data Entrants	Ezekwe Maureen C.
62	Data Entrants	Yusuf Fatima Imama
63	Data Entrants	Eyounghe Comfort Agbo
	KANO	
64	Data Entrants	Muwahib Bashir Nuhu
65	Data Entrants	Umar Lawan
66	Data Entrants	Salisu Awwal Salidu
67	Data Entrants	Lamin Ibrahim Usman
68	Data Entrants	Ilyasu Wada Bello