A PHASE 2, RANDOMIZED, OPEN-LABEL TRIAL TO DESCRIBE THE SAFETY AND IMMUNOGENICITY OF A MONOVALENT PNEUMOCOCCAL CONJUGATE CANDIDATE ADMINISTERED AS A 2-DOSE SERIES IN HEALTHY TODDLERS 11 THROUGH 15 MONTHS OF AGE WHO PREVIOUSLY RECEIVED THE PCV10 PRIMARY SERIES

Study Intervention Number:	PF-07831695
Study Intervention Name:	N/A
US IND Number:	N/A
EU CT Number:	2023-505154-18-00
ClinicalTrials.gov ID:	TBD
Pediatric Investigational Plan Number:	TBD
Protocol Number:	C4801002
Phase:	2
Sponsor Legal Address:	Pfizer Inc. 66 Hudson Boulevard East New York, NY 10001

Brief Title: A Phase 2 Safety and Immunogenicity Study of a Monovalent Pneumococcal Conjugate Candidate in Healthy Toddlers

Document History

Document	Version Date
Protocol Amendment 1	15 September 2023
Original protocol	31 May 2023

This amendment incorporates all revisions to date, including amendments made at the request of country health authorities and IRBs/ECs and any protocol administrative change letter(s).

Protocol Amendment Summary of Changes Table

Protocol Amendment 1 (15 September 2023)

Overall Rationale for the Amendment: To provide scientific rationale for participant selection and to provide further clarification regarding exploratory assays.

Description of Change.	Brief Rationale	Section # and Name
Non-substantial Modification(s)		
Added relevant data from publications and background information within the appropriate sections. Added subsection 4.2.2 "Rationale for Selection of Toddler Population"	To provide scientific justification for age of participants	Section 2.1 Study Rationale, Section 2.2 Background, Section 4.2 Scientific Rationale for Study Design
Added "immunogenicity" to "additional assessments"	To clarify that exploratory assays, if performed, are limited to only immunological assays.	Section 8.2 Efficacy and/or Immunogenicity Assessments

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1. PROTOCOL SUMMARY

1.1. Synopsis

Protocol Title: A Phase 2, Randomized, Open-Label Trial to Describe the Safety and Immunogenicity of a Monovalent Pneumococcal Conjugate Candidate Administered As a 2-Dose Series in Healthy Toddlers 11 Through 15 Months of Age Who Previously Received the PCV10 Primary Series

Brief Title: A Phase 2 Safety and Immunogenicity Study of a Monovalent Pneumococcal Conjugate Candidate in Healthy Toddlers

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Protocol Number:	C4801002
Phase:	2

Rationale:

Streptococcus pneumoniae causes invasive (eg, meningitis, sepsis, bacteremic pneumonia) and noninvasive (eg, otitis media [OM], nonbacteremic pneumonia, sinusitis) disease associated with significant healthcare burden, morbidity, and mortality. The 13-valent pneumococcal conjugate vaccine (Prevnar 13®; 13vPnC) was licensed more than a decade ago by the Food and Drug Administration (FDA) and other regulatory agencies around the world, including the European Medicines Agency (EMA), for use in infants and young children for the prevention of pneumococcal disease. The 20-valent pneumococcal conjugate vaccine (20vPnC) was developed to expand protection against pneumococcal invasive disease and pneumonia. The vaccine has been approved by the FDA and EMA for adults ≥18 years of age and is being developed for use in the pediatric population. 20vPnC contains the identical polysaccharide conjugates and excipients as 13vPnC but with conjugate polysaccharides for 7 additional serotypes.

Both 13vPnC and 20vPnC contain the same conjugate for serotype 3 (pneumococcal serotype 3 conjugate [PnC3]). Although there is evidence of direct protection by 13vPnC against invasive pneumococcal disease (IPD) and pneumonia due to serotype 3, serotype 3 still accounts for a majority of residual 13vPnC-type pneumococcal disease in children in countries that have introduced 13vPnC into their national immunization programs (NIPs). In children <5 years of age in the European Union (EU), 7% to 10% of IPD is caused by serotype 3. Therefore, there is an opportunity to evaluate new approaches that may enhance the immune response to this serotype. A Phase 1 study in adults was conducted to evaluate the safety and immunogenicity of different formulations to enhance serotype 3 immune

responses, including CCI modifications, use of an CCI , and CCI . The monovalent pneumococcal conjugate candidate (mPnC candidate) used in this study was selected for further development based on data from the Phase 1 study in adults. In the adult Phase 1 study, the CCI

This randomized, open-label, Phase 2 study is designed to describe the safety and immunogenicity of an mPnC candidate in children 11 through 15 months of age who have previously received the 2-dose 10-valent pneumococcal conjugate vaccine (PCV10) primary series as part of their infant routine vaccines. The current PnC3 formulation used in 13vPnC and 20vPnC will be used as direct comparator in this study. Data from this study will help inform the development of future multivalent pneumococcal conjugate vaccine (PCV) formulations.

Objectives, Endpoints, and Estimands:

Objectives	Endpoints	Estimands
Primary:	**Primary:**	**Primary:**
• To describe the safety profile of the mPnC candidate administered as a 2-dose series in children ≥11 to ≤15 months of age	• Prompted local reactions (redness, swelling, and pain at the injection site) • Prompted systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability) • Adverse events (AEs) • Serious adverse events (SAEs)	In participants receiving at least 1 dose of the study intervention from each group, the percentage of participants reporting: • Prompted local reactions within 7 days after each dose • Prompted systemic events within 7 days after each dose • AEs from Dose 1 through 1 month after Dose 2 • SAEs from Dose 1 through 1 month after Dose 2
Secondary:	**Secondary:**	**Secondary:**
• To describe the immune responses elicited by the mPnC candidate	• Immunoglobulin G (IgG) concentrations for the candidate serotype	In participants in compliance with the key protocol criteria (evaluable participants) from each group: • Pneumococcal IgG geometric mean concentrations (GMCs) 1 month after Dose 1 and 1 month after Dose 2 • Percentages of participants with predefined IgG concentration 1 month after Dose 1 and 1 month after Dose 2

Objectives	Endpoints	Estimands
		• Pneumococcal IgG geometric mean fold rises (GMFRs) from before Dose 1 to 1 month after Dose 1 and from 1 month after Dose 1 to 1 month after Dose 2
	• Opsonophagocytic activity (OPA) titers for the candidate serotype	• Pneumococcal OPA geometric mean titers (GMTs) 1 month after Dose 1 and 1 month after Dose 2 • Pneumococcal OPA GMFRs from before Dose 1 to 1 month after Dose 1 and from 1 month after Dose 1 to 1 month after Dose 2

Overall Design:

This is a Phase 2, multicenter, randomized, open-label study to describe the safety and immunogenicity of an mPnC candidate as a 2-dose series in healthy toddlers 11 through 15 months of age. This study will be conducted at investigator sites in the EU. Approximately 100 children between 11 and 15 months of age who previously received the 2-dose PCV10 infant primary series as part of their routine vaccines will be enrolled. Participants will be enrolled and randomized in a 1:1 ratio by site-based randomization to receive either the mPnC candidate or the control (mPnC control) as a 2-dose series at Visit 1 and Visit 3 (approximately 8 weeks apart); participants will receive the same study intervention for both doses. Participants will be observed for 30 minutes after each dose. Participants will also receive their toddler (third) dose of PCV10 concomitantly at Visit 1.

Other routine childhood vaccines as recommended by local standard of care may be administered during study participation. Prohibited vaccines are not allowed. Live vaccines may only be administered concomitantly with study intervention at Visit 1 and/or Visit 3 or be administered at least 28 days before or after study intervention administration.

Blood samples (~5 mL) will be collected at Visit 1 (prior to receiving Dose 1), Visit 2 (1 month after Dose 1), and Visit 4 (1 month after Dose 2). A total of 15 mL of blood will be collected from each participant during their study participation.

Local reactions at the study intervention injection site (redness, swelling, and pain at the injection site), systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability), and use of antipyretic/pain medication will be prompted for and collected by the participant's parent(s)/legal guardian in an e-diary, device or application, from Day 1 through Day 7 after each dose (where Day 1 is the day of study intervention administration).

AEs and SAEs will be collected from the signing of the informed consent document (ICD) through Visit 4 (1 month after Dose 2).

Number of Participants:

Approximately 100 participants (~50 per group) will be randomized to receive study intervention.

Study Population:

Key inclusion and exclusion criteria are listed below:

Key Inclusion Criteria

Participants must meet the following key inclusion criteria to be eligible for enrollment into the study:

- Toddlers ≥11 and ≤15 months of age at the time of consent.
- Have received exactly 2 infant doses of PCV10 according to a local immunization schedule.
- Healthy toddlers determined by clinical assessment, including medical history and clinical judgment, to be eligible for the study.

Key Exclusion Criteria

Participants with any of the following characteristics/conditions will be excluded:

- History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of study intervention, 13vPnC, 20vPnC, or any diphtheria toxoid–containing vaccine.
- Significant neurological disorder or history of seizure (excluding febrile seizure) or significant stable or evolving disorders such as cerebral palsy, encephalopathy, hydrocephalus, or other significant disorders.
- Major known congenital malformation or serious chronic disorder.
- History of microbiologically proven invasive disease caused by *S pneumoniae*.
- Previous vaccination with any licensed pneumococcal vaccine (other than the PCV10 primary infant series) or investigational pneumococcal vaccine, or planned receipt of nonstudy pneumococcal vaccine during study participation.

Study Arms and Duration:

Each participant will participate in the study for approximately 3 months (Visit 1 through Visit 4).

A 0.5-mL dose of mPnC candidate or a 0.5-mL dose of mPnC control will be administered intramuscularly into the left anterolateral thigh at Visit 1 and Visit 3. PCV10 will be administered into the right anterolateral thigh at Visit 1.

Other routine childhood vaccines as recommended by the local standard of care may be administered during study participation. Prohibited vaccines are not allowed. Live vaccines may only be administered concomitantly with study intervention at Visit 1 and/or Visit 3 or be administered at least 28 days before or after study intervention administration.

The study intervention (mPnC candidate and mPnC control) will be provided to the sites by the sponsor. PCV10 will be sourced locally by sites and sites will be reimbursed by the sponsor.

Study Intervention(s)			
Intervention Name	Conjugate candidate (CCI-µg/mL suspension with aluminum phosphate [$AlPO_4$])	Control (CCI-µg/mL suspension with $AlPO_4$)	PCV10
Type	Biologic	Biologic	Vaccine
Use	Experimental	Control	Standard of care (routine childhood vaccine)
Investigational Medicinal Product (IMP) or Noninvestigational Medicinal Product (NIMP)/Auxiliary Medicinal Product (AxMP)	IMP	IMP	AxMP
Dose Formulation	Preformulated solution for single-use injection	Preformulated solution for single-use injection	Single-use prefilled syringe (PFS) or in a vial (depending on sourcing)
Unit Dose Strength(s)	CCI µg/mL mPnC candidate	CCI µg/mL candidate control	1 µg of serotypes 1, 5, 6B, 7F, 9V, 14, and 23F, and 3 µg of serotypes 4, 18C, and 19F
Dosage Volume(s)	0.5 mL	0.5 mL	0.5 mL
Route of Administration	Intramuscular injection	Intramuscular injection	Intramuscular injection
Sourcing	Provided centrally by the sponsor	Provided centrally by the sponsor	Sourced locally

Study Intervention(s)			
Packaging and Labeling	Study intervention will be provided in a single-use vial. Each vial will be labeled as required per country requirement.	Study intervention will be provided in a vial. Each vial will be labeled as required per country requirement.	Study intervention will be provided in a PFS or in a vial. Each PFS or vial will be labeled as required per country requirement.
Single Reference Safety Document (SRSD)	Investigator's brochure (IB)	IB	Summary of product characteristics (SmPC)

Study Arm(s)		
Arm Title	mPnC candidate	mPnC control
Dose Level(s)	CCI µg mPnC candidate per 0.5-mL dose	CCI µg control per 0.5-mL dose
Arm Description	This study is an open-label study. Participants will receive the mPnC candidate at Visit 1 and Visit 3 (approximately 8 weeks apart). PCV10 will also be given at Visit 1.	This study is an open-label study. Participants will receive mPnC control at Visit 1 and Visit 3 (approximately 8 weeks apart). PCV10 will also be given at Visit 1.

Statistical Methods:

This is a Phase 2 open-label descriptive study with no formal statistical comparisons planned. The sample size of this study is not driven by any formal hypothesis test. Descriptive summary statistics will be provided for each safety and immunogenicity endpoint/estimand.

The primary objective is to describe the safety profile of the mPnC candidate. This will be done by summary statistics (including counts and percentages of participants and the associated 2-sided 95% CIs) for local reactions, systemic events, AEs, and SAEs for each group.

The secondary objective will be to describe the immunogenicity of the mPnC candidate. The IgG GMCs, IgG GMFRs, OPA GMTs, and OPA GMFRs at each applicable time point as well as the corresponding 95% CIs for each group will be provided. The descriptive statistics (including counts, percentages, and the associated 2-sided 95% CIs) for participants with predefined IgG concentrations of the candidate serotype will be provided for each group.

Ethical Considerations:

Participants enrolled in this study are from countries where the recommended infant PCV does not contain serotype 3. Receiving the mPnC candidate or mPnC control will not interfere with the standard of care for these participants and has the potential to provide additional protection.

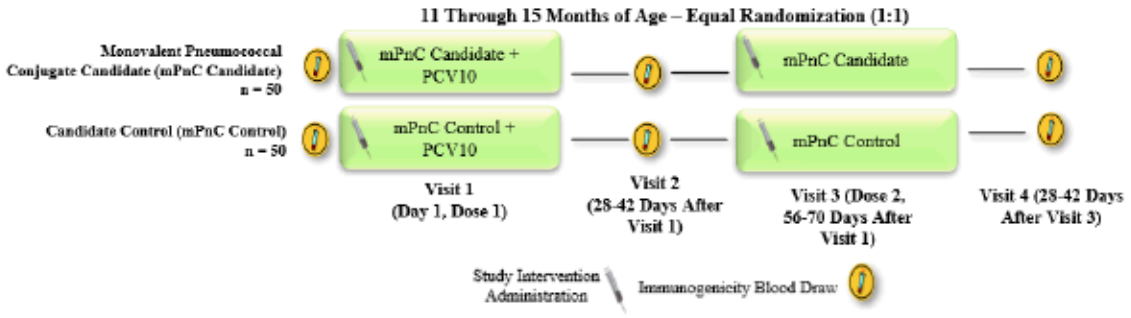
This study will be used to support the development of the mPnC candidate in future pneumococcal multivalent conjugate vaccines that could potentially benefit adults and children.

The mPnC candidate was evaluated in a Phase 1 adult study, exploring various CCI for serotype 3. CCI [redacted] Therefore, this mPnC candidate was selected for further development, which includes evaluation in the pediatric population. The data generated from this study will provide additional safety and immunogenicity data for future development.

The mPnC control used in this study is the serotype 3 CCI [redacted] used in the approved 13vPnC and 20vPnC and has an extensive safety history. The safety profile of mPnC control is expected to be similar to 13vPnC and 20vPnC.

The most common AEs in infants and toddlers after vaccination with 13vPnC or 20vPnC are primarily related to local reactions (injection site pain, redness, and swelling) and systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability). Safety reviews of data from the 5 completed Phase 3 20vPnC pediatric (infants and toddlers) trials, in addition to other pediatric 13vPnC trials, demonstrated an acceptable safety profile.

1.2. Schema



1.3. Schedule of Activities

The SoA table provides an overview of the protocol visits and procedures. Refer to the Study Assessments And Procedures section of the protocol for detailed information on each procedure and assessment required for compliance with the protocol.

The investigator may schedule visits (unplanned visits) in addition to those listed in the SoA table, in order to conduct evaluations or assessments required to protect the well-being of the participant.

Visit Number	1	2	3	4
Visit Description	**Dose 1 Visit**	**Dose 1 Follow-Up Visit**	**Dose 2 Visit**	**Dose 2 Follow-Up Visit**
Visit Type	**Clinic Visit**	**Clinic Visit**	**Clinic Visit**	**Clinic Visit**
Visit Window (Days)	**Day 1**	**28 to 42 Days After Visit 1**	**56 to 70 Days after Visit 1**	**28 to 42 Days After Visit 3**
Obtain informed consent	X			
Assign participant number via the IRT	X			
Record demography	X			
Perform clinical assessment, including medical history	X			
Record vaccine history, including prior PCV10 history	X			
Record nonstudy vaccinations and concomitant medications[a]	X	X	X	X
Obtain prevaccination temperature (measured as appropriate for age)	X		X	
Review inclusion and exclusion criteria	X			
Review temporary delay criteria	X		X	
Assign randomization number	X			
Review continued eligibility		X	X	
Obtain blood sample[b]	~5 mL	~5 mL		~5 mL
Administer study intervention (mPnC candidate or mPnC control)	X		X	
Administer PCV10	X			
If applicable, record administration of permitted concomitant vaccine(s) (refer to Section 6.9)	X	X	X	X
Observe and record immediate reactions for 30 minutes after study intervention administration	X		X	
Provide a participant contact card to parent or legal guardian	X			

Visit Number	1	2	3	4
Visit Description	Dose 1 Visit	Dose 1 Follow-Up Visit	Dose 2 Visit	Dose 2 Follow-Up Visit
Visit Type	Clinic Visit	Clinic Visit	Clinic Visit	Clinic Visit
Visit Window (Days)	Day 1	28 to 42 Days After Visit 1	56 to 70 Days after Visit 1	28 to 42 Days After Visit 3
Provide parent(s) or legal guardian with an e-diary (device or application), thermometer, and measuring device and instruct them to collect prompted local reactions and systemic events[c]	X		X (if needed)	
Review e-diary[d]	X----------X		X----------X	
Collect e-diary[e]				X
Record and report AEs and SAEs	X----------X			

a. Record concomitant medications used to treat SAEs.
b. Blood sample will be collected prior to administration if it is a study intervention administration visit.
c. The participant's parent(s)/legal guardian will record in an e-diary prompted local reactions and systemic events occurring within 7 days following each dose of study intervention. Use of antipyretic/pain medications will also be prompted for and collected daily in an e-diary for 7 days after each dose. The participant's parent(s)/legal guardian will be instructed to contact the study staff if the participant experiences redness or swelling measuring >14 device units, severe pain at the study intervention injection site, or a fever >40.0°C (>104.0°F) or has an emergency room visit or hospitalization.
d. Designated site staff will review e-diary data for the 7 days following each dose to evaluate participant compliance and reported events as part of the ongoing safety review.
e. Any e-diary devices given to participants' parents or legal guardians are to be collected at Visit 4.

2. INTRODUCTION

S pneumoniae causes invasive disease (eg, meningitis, sepsis, bacteremic pneumonia) and noninvasive disease (eg, OM, nonbacteremic pneumonia, sinusitis) associated with a significant healthcare burden, morbidity, and mortality.[1] The 13-valent pneumococcal conjugate vaccine (Prevnar 13; 13vPnC) was licensed more than a decade ago by the FDA and other regulatory agencies around the world, including the EMA, for use in infants and young children for the prevention of pneumococcal disease.[2,3] It was subsequently indicated for prevention of pneumonia in adults ≥18 years of age. 13vPnC has been introduced into NIPs for pediatric and adult populations worldwide.

Despite significant reductions in pneumococcal disease following use of 13vPnC, a significant burden of pneumococcal disease remains.[4] The pneumococcal 20-valent conjugate vaccine (20vPnC; Prevnar 20®) was developed to expand protection against IPD and pneumonia and has been approved by the FDA and EMA for adults ≥18 years of age. It is also being developed for pediatric patients. 20vPnC contains the identical polysaccharide conjugates and excipients as 13vPnC, but with conjugate polysaccharides for 7 additional serotypes.

Both 13vPnC and 20vPnC contain PnC3, and there is evidence of direct protection against IPD and pneumonia due to serotype 3.[5,6,7] However, serotype 3 still accounts for residual 13vPnC-type pneumococcal disease in countries that have introduced 13vPnC into their NIPs. Though there are a variety of factors that contribute to this, enhancing the immune response to serotype 3 may have an impact on residual disease burden.

2.1. Study Rationale

The burden of serotype 3 disease remains a problem in children. In European children, the VE of 13vPnC against serotype 3 IPD was 55% for fully vaccinated children (2+1 schedule in infants).[8] However, waning VE was observed in England and Wales for 13vPnC against IPD due to serotype 3 among older children 2 to 9 years of age, but not for the other 13vPnC serotypes beyond 7vPnC (excluding serotype 3).[9] Further, serotype 3 is now the most prevalent serotype causing IPD and OM in children <5 years of age in numerous countries around the world, including Germany (35% of OM cases in children <5 years of age) and Australia (28% of IPD cases in children <5 years of age).[10,11] Effectiveness may be impacted by the physical properties of the polysaccharide capsule that are unique among most other serotypes as the polysaccharide structure facilitates immune evasion by shedding the capsule, the primary binding site of neutralizing antibody.[12] Modification of the current formulation may overcome these attributes to induce a stronger immune response that could provide greater protection in vaccinated populations.

The purpose of the study is to describe the safety and immunogenicity of an mPnC candidate as a 2-dose series in toddlers who previously received PCV10 as a 2-dose primary series. The safety and immunogenicity results from this study will contribute to future development of pneumococcal vaccine formulations.

2.2. Background

Preclinical studies have demonstrated that modifying the approach to manufacturing serotype 3 conjugates substantially increases the levels of antibody elicited. This increase in immune response seen in novel PnC3 candidates, if incorporated as part of a next-generation pneumococcal vaccine, may provide greater protection in vaccinated populations, particularly in infants and toddlers who are at highest risk for IPD.[4]

A Phase 1 study in adults was conducted to evaluate different formulations that included changes to CCI [redacted], and/or CCI [redacted] Therefore, this mPnC candidate was selected for further development, which includes evaluation in the pediatric population.

2.2.1. Clinical Overview

The mPnC candidate selected for use in this study has modifications to the CCI [redacted] the CCI [redacted], and the CCI [redacted] when compared to the original serotype formulation found in 13vPnC and 20vPnC. These modifications can increase the immune response and impact conjugate stability and immunogenicity (see the IB for details).

CCI [redacted]

2.3. Benefit/Risk Assessment

Participants will be enrolled in this study from countries where the recommended infant PCV does not contain serotype 3. Receiving the mPnC candidate or mPnC control will not interfere with the standard of care for these participants and has the potential to provide additional protection.

This study will be used to support the development of future pneumococcal multivalent conjugate vaccines that could potentially benefit adults and children.

The mPnC control used in this study is the serotype 3 conjugate used in the approved 13vPnC and 20vPnC and has an extensive safety history. The safety profile of mPnC control is expected to be similar to 13vPnC and 20vPnC.

The most common AEs noted in infants and toddlers after vaccination with 13vPnC and 20vPnC are primarily related to local reactions (injection site pain, redness, and swelling) and systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability). Safety reviews of data from the 5 completed Phase 3 20vPnC pediatric (infants and toddlers) trials, in addition to other pediatric 13vPnC trials, revealed no safety concerns.

As with any vaccine, an allergic reaction can occur. The allergic reaction can vary from skin rash to swelling of the face or lips, wheezing, and/or shortness of breath. A severe allergic reaction (anaphylactic shock, collapse, or shock-like state [hypotonic-hyporesponsive episode]) may also occur. There may also be additional risks related to the vaccines administered in the study that are not known at this time.

Additional potential risks of clinical significance are presented in the table in Section 2.3.1.

More detailed information about the known and expected benefits and risks and reasonably expected AEs of the mPnC candidate and mPnC control may be found in the IB, which is the SRSD for this study. For PCV10, the SRSD will be the SmPC.

2.3.1. Risk Assessment

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
Study Intervention(s): mPnC candidate and mPnC control		
The safety profile of the mPnC candidate is not yet fully characterized. Local and systemic reactions to the investigational serotype candidate may occur (injection site redness, injection site swelling, and injection site pain; fever, decreased appetite, increased sleep/drowsiness, and irritability) following study intervention.	The mPnC candidate risks are unknown. The potential risks are detailed in the IB.	• Eligibility criteria have been selected to ensure that only appropriate participants are included in the study (see Section 5.1 and Section 5.2). • All study participants will be observed for 30 minutes after study intervention administration. • E-diary and AE data will be monitored by the investigator (or designee) and sponsor.
Concomitant Vaccine: PCV10		
The relevant key risks associated with PCV10 include local reactions (injection site pain, redness, and swelling) and systemic events (fever, decreased appetite, increased sleep/drowsiness, and irritability). Uncommon events can include allergic reactions, which may be associated with skin rash, face or lip swelling, wheezing, shortness of breath, or rare severe allergic reactions (eg, anaphylactic shock).	The risks are derived from the related PCV10 clinical trials and postmarketing data and the clinical data described in the PCV10 SmPC.	• Eligibility criteria have been selected to ensure that only appropriate participants are included in the study see Section 5.1 and Section 5.2). • All study participants will be observed for 30 minutes after vaccination. • E-diary and AE data will be monitored by the investigator (or designee) and sponsor.
Study Procedures: Venipuncture		
Venipuncture is required to collect immunogenicity data from participants.	There is the risk of fainting, and pain, swelling, bruising, and infection at the venipuncture site.	Only qualified nurses, physicians, nurse practitioners, physician assistants, phlebotomists, or medical assistants certified or otherwise authorized to draw blood per the standards and procedures of the investigative site, as allowed by institutional, local, and country guidance, will be allowed to draw blood, to minimize local complications.

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
Other		
Participants and their caregivers will be required to attend healthcare facilities during the global SARS-CoV-2 pandemic.	Without appropriate social distancing and PPE, there is a potential for increased exposure to SARS-CoV-2.	Pfizer will work with sites to ensure an appropriate COVID-19 prevention strategy. Monitoring for cases of COVID-19 during the study as part of the COVID-19 surveillance.

2.3.2. Benefit Assessment

Participants in clinical studies may not directly benefit from participation, as clinical studies are designed to provide information about the safety and immunogenicity of an investigational vaccine. Joining this study will be contributing to research to help others. The mPnC candidate could be used in a future investigational expanded-valent PCV. A safe and immunogenic PCV with expanded pneumococcal serotype coverage would fulfill an unmet need for expanded protection against pneumococcal disease.

2.3.3. Overall Benefit/Risk Conclusion

Participants enrolled in this study are from countries where the recommended infant PCV provided does not contain serotype 3. Receiving the mPnC candidate or mPnC control will not interfere with standard of care for these participants and has the potential to provide additional protection.

This study will be used to support the development of future pneumococcal multivalent conjugate vaccines that could potentially benefit adults and children.

Considering the measures to minimize risk to study participants, the potential risks identified in association with the mPnC candidate are justified by the potential benefits that may be afforded to participants who may be at risk of IPD due to their young age.

3. OBJECTIVES, ENDPOINTS, AND ESTIMANDS

Objectives	Endpoints	Estimands
Primary:	**Primary:**	**Primary:**
• To describe the safety profile of the mPnC candidate administered as a 2-dose series in children ≥11 to ≤15 months of age	• Prompted local reactions (redness, swelling, and pain at the injection site) • Prompted systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability) • AEs • SAEs	In participants receiving at least 1 dose of the study intervention from each group, the percentage of participants reporting: • Prompted local reactions within 7 days after each dose • Prompted systemic events within 7 days after each dose • AEs from Dose 1 through 1 month after Dose 2 • SAEs from Dose 1 through 1 month after Dose 2
Secondary:	**Secondary:**	**Secondary:**
• To describe the immune responses elicited by the mPnC candidate	• IgG concentrations for the candidate serotype	In participants in compliance with the key protocol criteria (evaluable participants) from each group: • Pneumococcal IgG GMCs 1 month after Dose 1 and 1 month after Dose 2 • Percentages of participants with predefined IgG concentration 1 month after Dose 1 and 1 month after Dose 2

Objectives	Endpoints	Estimands
		• Pneumococcal IgG GMFRs from before Dose 1 to 1 month after Dose 1 and from 1 month after Dose 1 to 1 month after Dose 2
	• OPA titers for the candidate serotype	• Pneumococcal OPA GMTs 1 month after Dose 1 and 1 month after Dose 2 • Pneumococcal OPA GMFRs from before Dose 1 to 1 month after Dose 1 and from 1 month after Dose 1 to 1 month after Dose 2
Exploratory:	**Exploratory:**	**Exploratory:**
[redacted]	• To be described in the SAP	• To be described in the SAP

4. STUDY DESIGN

4.1. Overall Design

This is a Phase 2, multicenter, randomized, open-label study to describe the safety and immunogenicity of an mPnC candidate as a 2-dose series in healthy toddlers 11 through 15 months of age. This study will be conducted at investigator sites in the EU. Approximately 100 children between 11 and 15 months of age who previously received the 2-dose PCV10 infant primary series as part of their routine vaccines will be enrolled. Participants will be enrolled and randomized in a 1:1 ratio by site-based randomization to receive either the mPnC candidate or the control (mPnC control) as a 2-dose series at Visit 1 and Visit 3; participants will receive the same study intervention (either mPnC candidate or mPnC control) for both doses. Participants will be observed for 30 minutes after each dose. Participants will also receive their toddler (third) dose of PCV10 concomitantly at Visit 1.

Other routine childhood vaccines as recommended by local standard of care may be administered during study participation. Prohibited vaccines (see Section 6.9.1) are not allowed. Live vaccines may only be administered concomitantly with study intervention at Visit 1 and/or Visit 3 or be administered at least 28 days before or after study intervention administration (see Section 6.9.2).

On Day 1 (Visit 1), participants will be assessed for eligibility, have information collected, including medical history and vaccine history, and have blood drawn (~5 mL) for immunogenicity assessments prior to receiving their study intervention and PCV10. Temperature, measured as appropriate for the participant's age, will be taken, and temporary delay criteria will be reviewed prior to study intervention administration. Upon confirmation of eligibility, participants will be randomized to receive Dose 1 of the mPnC candidate or the mPnC control, as well as their toddler dose of PCV10. Study intervention (mPnC candidate or mPnC control) will be administered intramuscularly into the left anterolateral thigh, while PCV10 will be administered intramuscularly into the right anterolateral thigh. Other routine

childhood vaccines, if allowed (see Section 6.9), may be administered at this visit into a different limb other than the site of the study intervention injection. Participants will be observed for 30 minutes after administration of study intervention and any reactions occurring during that time will be recorded as AEs. The parent(s)/legal guardian will be provided with an e-diary (or e-diary application), thermometer, and measuring device and instructed to collect prompted local reactions (redness, swelling, and pain at the injection site) and prompted systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability) occurring within 7 days after administration of study intervention. Use of antipyretic/pain medications will also be prompted for and collected daily in the e-diary for 7 days after administration of study intervention. The participant's parent(s)/legal guardian will be instructed to contact the study staff if the participant experiences redness or swelling >14 caliper units (>7 cm), severe pain at the study intervention injection site, or fever >40.0°C (>104.0°F) or has an emergency room visit or hospitalization in the 7 days after vaccination.

At Visit 2 (28-42 days after Visit 1), participants will return for follow-up and blood draw. Information will be collected from the participants' parents/legal guardians on AEs, SAEs, and e-diary follow-up (as needed). Concomitant medications used to treat SAEs will be recorded. Information on vaccines administered since the last visit will also be recorded to ensure that the participant did not receive prohibited vaccine(s) during this period. Blood (~5 mL) will be drawn for immunogenicity assessments. Other routine childhood vaccines, if allowed (see Section 6.9), may be administered at this visit. If applicable, remind the parent(s)/legal guardian to bring e-diary device for the next visit.

At Visit 3 (56-70 days after Visit 1), participants will return for Dose 2. Participants will be assessed for continued eligibility and information will be collected from the participants' parents/legal guardians on AEs, including nonserious AEs and SAEs. Concomitant medications used to treat SAEs will be recorded. Information on vaccines administered since the last visit will also be recorded. Temperature, measured as appropriate for the participant's age, will be taken, and temporary delay criteria will be reviewed prior to study intervention administration. Participants with continued eligibility will be administered Dose 2 into the left anterolateral thigh, observed for 30 minutes, and given the same instructions as in Visit 1. Other routine childhood vaccines, if allowed (see Section 6.9), may be administered at this visit into a different limb other than the site of the study intervention injection.

The parent(s)/legal guardian will be instructed to collect prompted local reactions and systemic events occurring within 7 days after administration of study intervention using the e-diary device provided at Visit 1 (or e-diary application downloaded at Visit 1).

Use of antipyretic/pain medications will also be prompted for and collected daily in the e-diary for 7 days after administration of study intervention. The participant's parent(s)/legal guardian will be instructed to contact the study staff if the participant experiences redness or swelling >14 caliper units, severe pain at the study intervention injection site, or fever >40.0°C (>104.0°F) or has an emergency room visit or hospitalization.

At Visit 4 (28-42 days after Visit 3), participants will return for follow-up and blood draw. Information will be collected from the participants' parents/legal guardians on AEs, SAEs, and e-diary follow-up (as needed). Concomitant medications used to treat SAEs will be recorded. Information on vaccines administered since the last visit will be reviewed. Blood (~5 mL) will be drawn for immunogenicity assessments. Other routine childhood vaccines, if allowed (see Section 6.9), may be administered at this visit. The e-diary device will be collected, if applicable.

4.2. Scientific Rationale for Study Design

4.2.1. Country Selection

The study will be conducted in countries where PCV10 is part of the NIP, as PCV10 does not contain pneumococcal serotype 3 conjugate.

4.2.2. Rationale for Selection of Toddler Population

Toddlers 11 through 15 months of age are the selected population for this study for several reasons. Infants and toddlers have poor immune responses to polysaccharide vaccines, such as PPSV23, because the polysaccharide antigen elicits a T-independent immune response that requires specialized marginal-zone B cells, which develop after 2 years of age.[13] Conjugation of an immunogenic protein to a bacterial capsular polysaccharide converts the T-independent polysaccharide antigen into a T-dependent antigen capable of eliciting robust antibody responses in children <2 years of age. Thus, due to the specific limitations in the infant/toddler immune response to polysaccharide antigens, it is necessary to evaluate the ability of the mPnC candidate to perform as a polysaccharide conjugate vaccine in this population.

The 11 to 15 months age range aligns with national recommendations for PCV booster doses in the relevant countries where the study is conducted, and PCV10 is recommended in the NIP. Importantly for the objectives of the study, PCV10 does not include serotype 3. Therefore, toddlers participating in the study will be immunologically naïve to serotype 3 vaccination, thus enabling evaluation of primary responses to the mPnC study intervention.

Furthermore, the risk of IPD and the need for its optimal prevention is the highest in the infant and young child (≤4 years of age) age group.[4] Pneumococcal carriage rates peak in this age group, driving serotype 3 disease prevalence and transmission within this age group and older children and adults.[14] Therefore, improved serotype 3 responses with the potential for decreased nasopharyngeal carriage in this population could substantially impact the overall incidence of disease and herd immunity at a population level.

Finally, robust safety data from the adult Phase 1 study and preclinical studies (see Section 2.2 and the IB for details) support the selection of this population in this Phase 2 trial.

4.2.3. Rationale for Comparator

This study will use a direct comparator, mPnC control, which is the current formulation for serotype 3 used in the approved 13vPnC and 20vPnC vaccines. The mPnC control contains [redacted] µg of [redacted] for serotype 3 and uses [redacted] with [redacted]

4.3. Justification for Dose

The mPnC candidate was evaluated in a Phase 1 adult study that explored various [redacted] for mPnC3. [redacted] Therefore, this mPnC candidate was selected for further development, which includes evaluation in the pediatric population.

The mPnC candidate contains [redacted] µg/dose of serotype 3 polysaccharide using the [redacted] with [redacted].

[redacted] In dose-ranging studies with investigational vaccines and with 13vPnC, immune responses were at times higher, but not consistently, leaving dose-response to remain in question. The safety profile was acceptable even at the highest doses in these studies.[15,16,17]

The highest doses of the mPnC candidate have been tested in nonclinical toxicity studies (see the IB for details). No significant adverse effects were seen with animal data in rats at the highest dose range.

4.4. End of Study Definition

The end of the study is defined as the date of the last visit of the last participant in the study.

A participant is considered to have completed the study if they have completed all periods of the study, including the last visit.

5. STUDY POPULATION

This study can fulfill its objectives only if appropriate participants are enrolled, including participants across diverse and representative racial and ethnic backgrounds. If a prescreening tool is utilized for study recruitment purposes, it will include collection of information that reflects the enrollment of a diverse participant population including, where permitted under local regulations, age, sex, race, and ethnicity. The following eligibility criteria are designed to select participants for whom participation in the study is considered appropriate. All relevant medical and nonmedical conditions should be taken into consideration when deciding whether a particular participant is suitable for this protocol.

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

5.1. Inclusion Criteria

Participants are eligible to be included in this study only if all of the following criteria apply:

Age and Sex:

1. Toddlers ≥11 to ≤15 months of age at the time of consent.

Disease Characteristics:

2. Have received exactly 2 infant doses of PCV10 according to a local immunization schedule. Documented confirmation of PCV10 receipt will be collected prior to randomization. The last dose of PCV10 must have been administered >56 days before enrollment into the study.

Other Inclusion Criteria:

3. Participants whose parent(s)/legal guardian is willing and able to comply with all scheduled in-clinic visits, study schedule, and other study procedures, including blood draws.

4. Healthy toddlers determined by clinical assessment, including medical history and clinical judgment, to be eligible for the study.

5. Expected to be available for the duration of the study and whose parent(s)/legal guardian can be contacted by telephone during study participation.

6. Participants whose parent(s)/legal guardian is capable of giving signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol.

5.2. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

Medical Conditions:

1. History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention, 13vPnC, 20vPnC, or any diphtheria toxoid-containing vaccine.

2. Significant neurological disorder or history of seizure (excluding febrile seizure) or significant stable or evolving disorders such as cerebral palsy, encephalopathy, hydrocephalus, or other significant disorders.

3. Major known congenital malformation or serious chronic disorder.

4. History of microbiologically proven invasive disease caused by *S pneumoniae.*

5. Known or suspected immunodeficiency or other conditions associated with immunosuppression, including, but not limited to, immunoglobulin class/subclass deficiencies, DiGeorge syndrome, generalized malignancy, HIV infection, leukemia, lymphoma, or organ or bone marrow transplant.

6. Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.

7. Congenital, functional, or surgical asplenia.

8. Other medical condition or laboratory abnormality that may increase the risk of study participation or study intervention administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the participant inappropriate for entry into this study.

9. Previous vaccination with any licensed pneumococcal vaccine (other than the PCV10 primary infant series) or investigational pneumococcal vaccine, or planned receipt of nonstudy pneumococcal vaccine during study participation.

10. Currently receives treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, or planned receipt through the last blood draw. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled in the study until corticosteroid therapy has been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized, intra-articular, intrabursal, or topical (eg, skin, eyes, or ears) corticosteroids are permitted.

11. Receipt of blood/plasma products or immunoglobulins (including hepatitis B immunoglobulin) or planned receipt through the last planned blood draw in the study (through Visit 4).

Prior/Concurrent Clinical Study Experience:

12. Participation in other studies involving investigational drug(s), investigational vaccines, or investigational devices within 28 days prior to study entry and/or during study participation or intrauterine exposure to investigational vaccines. An exception to this is an investigational vaccine authorized by the national regulatory agency for use in infants or toddlers to prevent pandemic disease. Participation in purely observational studies is acceptable.

Diagnostic Assessments:

Not applicable.

Other Exclusion Criteria:

13. Children or grandchildren who are direct descendants of investigator site staff or sponsor and sponsor delegate employees directly involved in the conduct of the study.

5.3. Lifestyle Considerations

Not applicable. No restrictions are required.

5.4. Screen Failures

Screen failures are defined as participants whose parents/legal guardians have consented for them to participate in the clinical study but are not subsequently randomly assigned to study intervention. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants to meet the CONSORT publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any SAEs recorded from signing the informed consent until the time of determination of screen failures.

Individuals who do not meet the criteria for participation in this study (screen failures) may not be rescreened.

5.5. Criteria for Temporarily Delaying Enrollment/Randomization/Administration of Study Intervention

The following conditions are temporary or self-limiting and a participant may be vaccinated once the condition(s) has/have resolved, and no other exclusion criteria are met.

The blood draws prior to administration of study intervention should take place on the same day as the administration of study intervention.

- Current febrile illness (body temperature ≥38.0°C [≥100.4°F]) or other acute illness within 48 hours before study intervention administration.
- Receipt of any live vaccine within 28 days before study intervention administration or anticipate receipt of any live vaccine within 28 days after study intervention administration.
    - Licensed live vaccine(s) administered on the same day as study intervention at Visit 1 and/or Visit 3 is/are permitted (Section 6.9.2).

- Receipt of short-term (<14 days) systemic corticosteroids. Study intervention administration should be delayed until systemic corticosteroid use has been discontinued for at least 28 days. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin, eyes, or ears) corticosteroids are permitted.

6. STUDY INTERVENTION(S) AND CONCOMITANT THERAPY

Study interventions are all prespecified investigational and noninvestigational medicinal products, medical devices, and other interventions (eg, surgical and behavioral) intended to be administered to the study participants during the study conduct.

For the purposes of this protocol, study intervention refers to the mPnC candidate and the mPnC control. PCV10 is not considered to be a study intervention.

Study interventions will be provided as 2 preformulated products in vials, and PCV10 may be provided as a PFS or in a vial, as outlined below:

- PF-07831695 suspension for injection with $AlPO_4$, CCI µg/mL, 0.5-mL vial (CCI) (mPnC control)
- PF-07831695 suspension for injection with $AlPO_4$, CCI µg/mL, 0.5-mL vial (CCI) (mPnC candidate)
- PCV10 (Synflorix) (PFS or in a vial)

The study interventions will be prepared by adjusting the volume extracted from the preformulated products in vials to a dose of 0.5 mL. PCV10 will be administered as a 0.5-mL dose.

6.1. Study Intervention(s) Administered

Study Intervention(s)			
Intervention Name	mPnC candidate (CCI -µg/mL suspension with $AlPO_4$)	Control (CCI -µg/mL suspension with $AlPO_4$)	PCV10
Type	Biologic	Biologic	Vaccine
Use	Experimental	Control	Standard of care (routine childhood vaccine)
IMP or NIMP/AxMP	IMP	IMP	AxMP
Dose Formulation	Preformulated solution for single-use injection	Preformulated solution for single-use injection	Single-use PFS or in a vial (depending on sourcing)

Study Intervention(s)			
Unit Dose Strength(s)	CCI µg/mL mPnC candidate	CCI µg/mL control	1 µg of serotypes 1, 5, 6B, 7F, 9V, 14, and 23F, and 3 µg of serotypes 4, 18C, and 19F
Dosage Volume(s)	0.5 mL	0.5 mL	0.5 mL
Route of Administration	Intramuscular injection	Intramuscular injection	Intramuscular injection
Sourcing	Provided centrally by the sponsor	Provided centrally by the sponsor	Sourced locally
Packaging and Labeling	Study intervention will be provided in a single-use vial. Each vial will be labeled as required per country requirement.	Study intervention will be provided in a vial. Each vial will be labeled as required per country requirement.	Study intervention will be provided in a PFS or in a vial. Each PFS or vial will be labeled as required per country requirement.
SRSD	IB	IB	SmPC

Study Arm(s)		
Arm Title	mPnC candidate	mPnC control
Dose Level(s)	CCI µg mPnC candidate per 0.5-mL dose	CCI µg control per 0.5-mL dose
Arm Description	This study is an open-label study. Participants will receive the mPnC candidate at Visit 1 and Visit 3 (approximately 8 weeks apart). PCV10 will also be given at Visit 1. For other routine vaccines, refer to Section 6.9 for details.	This study is an open-label study. Participants will receive the mPnC control at Visit 1 and Visit 3 (approximately 8 weeks apart). PCV10 will also be given at Visit 1. For other routine vaccines, refer to Section 6.9 for details.

6.1.1. Administration

All participants will be administered either the mPnC candidate or mPnC control as assigned at Visit 1 and Visit 3. Participants will also receive their third dose of PCV10 at Visit 1.

Study interventions will be provided by the sponsor to the study sites. A 0.5-mL dose of the mPnC candidate or mPnC control will be administered intramuscularly in the left anterolateral thigh by a qualified site staff member at Visit 1 and Visit 3. The description of the mPnC candidate or mPnC control can be found in the IPM.

PCV10 will be sourced locally by sites and sites will be reimbursed by the sponsor. PCV10 will be administered intramuscularly in the right anterolateral thigh by a qualified staff member at Visit 1.

Any concomitant vaccines required by local recommendations and permitted by the protocol may be administered during study participation (see Section 6.9 for details).

Standard vaccination practices must be observed, and vaccine must not be injected into blood vessels. Appropriate medication and other supportive measures for management of an acute hypersensitivity reaction must be available in accordance with local guidelines for standard immunization practices.

Administration of study interventions will be performed by an appropriately qualified, trained, and vaccine-experienced member of the study staff (eg, physician, nurse, physician's assistant, nurse practitioner, pharmacist, or medical assistant) as allowed by local, state, and institutional guidance.

Study intervention administration details will be recorded on the CRF.

6.1.2. Medical Devices (if PCV10 Is Supplied in PFSs)

1. In this study, the medical devices being deployed are the PFSs containing PCV10.

2. Instructions for medical device use are provided in the package insert.

3. All medical device deficiencies (including malfunctions of the device, use error, and inadequate labeling) must be detected, documented, and reported by the study personnel throughout the study. Please refer to Section 8.4.9 for details.

6.2. Preparation, Handling, Storage, and Accountability

1. The investigator or designee must confirm that appropriate conditions (eg, temperature) have been maintained during transit for all study interventions received and any discrepancies are reported and resolved before use of the study intervention.

2. Only participants enrolled in the study may receive study intervention and only authorized site staff may supply, prepare, and/or administer study intervention.

3. All study interventions must be stored in a secure, environmentally controlled, and monitored (manual or automated recording) area in accordance with the labeled storage conditions with access limited to the investigator and authorized site staff. At a minimum, daily minimum and maximum temperatures for all site storage locations must be documented and available upon request. Data for nonworking days must indicate the minimum and maximum temperatures since previously documented upon return to business.

4. Any excursions from the study intervention label storage conditions should be reported to Pfizer upon discovery along with actions taken. The site should actively pursue options for returning the study intervention to labeled storage conditions, as soon as possible. Once an excursion is identified, the study intervention must be quarantined and not used until Pfizer provides permission to use the study intervention. Specific details regarding

the excursion definition and information to report for each excursion will be provided to the site in the IPM.

5. Any storage conditions stated in the SRSD will be superseded by the storage conditions stated on the label.

6. Study interventions should be stored in their original containers.

7. The investigator, institution, head of the medical institution (where applicable), or authorized site staff is responsible for study intervention accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records), such as the IPAL or sponsor-approved equivalent. All study interventions will be accounted for using a study intervention accountability form/record.

8. Further guidance and information for the final disposition of unused study interventions are provided in the IPM. All destruction must be adequately documented. If destruction is authorized to take place at the investigator site, the investigator must ensure that the materials are destroyed in compliance with applicable environmental regulations, institutional policy, and any special instructions provided by Pfizer.

Upon identification of a product complaint, notify the sponsor within 1 business day of discovery as described in the IPM.

6.2.1. Preparation and Dispensing

See the IPM for instructions on how to prepare the study intervention for administration. Study intervention should be prepared and dispensed by an appropriately qualified and experienced member of the study staff (eg, physician, nurse, physician's assistant, nurse practitioner, pharmacy assistant/technician, or pharmacist) as allowed by local, state, and institutional guidance. A second staff member will verify the dispensing.

The study intervention will be prepared by qualified site personnel according to the IPM.

6.3. Assignment to Study Intervention

Study intervention will be dispensed at the study visits summarized in the SoA.

Allocation (randomization) of participants to intervention groups will proceed through the use of an IRT system (IWR). The site personnel (study coordinator or specified designee) will be required to enter or select information including but not limited to the user's ID and password, the protocol number, and the participant number.

The study intervention to be dispensed to the participant will be assigned using an IRT system. The IRT system will provide a confirmation report containing the participant number, the randomization number, and DU or container number assigned. The confirmation report must be stored in the site's files. The site will record the study intervention assignment on the applicable CRF, if required.

This is an open-label study. The investigator's knowledge of the vaccine assignment must not influence the decision to enroll a particular participant or affect the order in which participants are enrolled. Potential bias will be reduced by central randomization.

The study-specific IRT reference manual and IPM will provide the contact information and further details on the use of the IRT system.

6.4. Blinding

This is an open-label study.

6.4.1. Blinding of Participants

Participants' caregivers will be unblinded to the participant's assigned study intervention.

6.4.2. Blinding of Site Personnel

Investigators and other site staff will be unblinded to participants' assigned study intervention.

6.4.3. Blinding of the Sponsor

Sponsor staff will be unblinded to participants' assigned study intervention. All laboratory testing personnel performing serology assays will remain blinded to study intervention assigned/received throughout the study.

As this is an open-label study, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessment and/or supporting clinical development.

6.5. Study Intervention Compliance

When participants are dosed at the site, they will receive study intervention directly from the investigator or designee, under medical supervision. The date and time of each dose administered in the clinic will be recorded in the source documents and recorded in the CRF. The dose of study intervention and study participant identification will be confirmed at the time of dosing by a member of the study site staff other than the person administering the study intervention.

The site will complete the required dosage Preparation Record located in the IPM. The use of the Preparation Record is required. The use of alternative preparation records must be approved by the sponsor's clinical research pharmacist prior to its use.

6.6. Dose Modification

Not applicable. Dose modification is not permitted during the study.

6.7. Continued Access to Study Intervention After the End of the Study

No study intervention will be provided to participants at the end of their study participation.

6.8. Treatment of Overdose

For this study, any dose of study intervention greater than 0.5 mL within a 24-hour time period will be considered an overdose.

There is no specific treatment for an overdose.

In the event of an overdose, the investigator should:

1. Contact the study medical monitor within 24 hours.
2. Closely monitor the participant for any AEs/SAEs as medically appropriate and follow up until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).
3. Document the quantity of the excess dose as well as the duration of the overdose in the CRF.
4. Overdose is reportable to Pfizer Safety **only when associated with an SAE.**

Decisions regarding dose interruptions or modifications will be made by the investigator in consultation with the study medical monitor as needed based on the clinical evaluation of the participant.

6.9. Prior and Concomitant Therapy

The name and date of administration for all nonstudy vaccinations received from 28 days prior to Visit 1 through Visit 4 will be collected and recorded in the CRF.

Medications taken to treat SAEs from the time of signing of the ICD through Visit 4 will be recorded in the CRF.

6.9.1. Prohibited During the Study

- Receipt of any investigational vaccines, drugs, or medical devices is prohibited during study participation.
- Receipt of nonstudy pneumococcal vaccine is prohibited during study participation.
- Receipt of meningococcal conjugate vaccine is prohibited during study participation.
- Receipt of blood/plasma products, immunoglobulins, and/or immunosuppressive therapy (including a ≥14-day course of systemic corticosteroids) is prohibited during study participation.

6.9.2. Permitted Concomitant Vaccines and Treatments

- Receipt of other licensed nonstudy vaccines as recommended by local standard of care (except pneumococcal and meningococcal vaccines described above) is permitted. Live vaccine(s) must be administered concomitantly with study intervention at Visit 1 and/or Visit 3, or at least 28 days before or after study intervention administration.
    - Licensed inactivated influenza vaccine may be given at any time throughout study participation, per official local recommendations/regulations.
- Prescription and nonprescription medications, vitamins, minerals, and herbal remedies are permitted during participation in the study.
- The use of prophylactic antipyretic/pain medication, while permitted, is not recommended on the day of study intervention administration (before or after administration of study intervention). If symptoms develop, the use of antipyretic/pain medication is allowed.
- Topical anesthetic at the site of blood draw is permitted.
- Inhaled/nebulized, topical (eg, skin, eyes, ears), or localized injections of corticosteroids (eg, intra-articular or intrabursal administration) are permitted during study participation.
- If medically necessary (eg, during a pandemic), a COVID-19 vaccine, or tetanus vaccine required following wound care, may be given during the study, with preference for >7 days after study intervention administration, if feasible.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

It may be necessary for a participant to permanently discontinue study intervention. Reasons for permanent discontinuation of study intervention include the following:

- Refused further study procedures;
- Lost to follow-up;
- Death;
- Study terminated by sponsor;
- AE;
- Physician decision;
- Protocol deviation;
- Screen failure;

- Withdrawal by parent/legal guardian;
- Vaccination error without associated AE;
- No longer meets eligibility criteria;
- Other.

Discontinuation of study intervention does not represent withdrawal from the study. If study intervention is permanently discontinued, the participant should remain in the study to be evaluated for safety follow-up. See the SoA for data to be collected at the time of discontinuation of study intervention and follow-up for any further evaluations that need to be completed.

In the event of discontinuation of study intervention, it must be documented on the appropriate CRF/in the medical records whether the participant is discontinuing further receipt of study intervention or also from study procedures, further study follow-up, and/or future collection of additional information.

7.2. Participant Discontinuation/Withdrawal From the Study

A participant may withdraw from the study at any time at their own request. Reasons for discontinuation from the study include the following:

- Refused further study procedures;
- Lost to follow-up;
- Death;
- Study terminated by sponsor;
- AE;
- Physician decision;
- Protocol deviation;
- Screen failure;
- Withdrawal by parent/legal guardian;
- Vaccination error without associated AE;
- No longer meets eligibility criteria;
- Other.

If a participant's parent(s)/legal guardian withdraws the participant from the study, the parent(s)/legal guardian may request destruction of any remaining samples taken and not tested, and the investigator must document any such requests in the site study records and notify the sponsor accordingly.

If the participant's parent(s)/legal guardian withdraws the participant from the study and also withdraws consent (see Section 7.2.1) for disclosure of future information, no further evaluations will be performed and no additional data will be collected. The sponsor may retain and continue to use any data collected before such withdrawal of consent.

7.2.1. Withdrawal of Consent

A participant whose parent(s)/legal guardian requests to discontinue receipt of study intervention will remain in the study and must continue to be followed for protocol-specified follow-up procedures. The only exception to this is when a participant's parent(s)/legal guardian specifically withdraws consent for any further contact with them or persons previously authorized by the participant to provide this information. A participant's parent(s)/legal guardian should notify the investigator in writing of the decision to withdraw consent from future follow-up, whenever possible. The withdrawal of consent should be explained in detail in the medical records by the investigator, as to whether the withdrawal is only from further receipt of study intervention or also from study procedures and/or postdose study follow-up and entered on the appropriate CRF page. In the event that vital status (whether the participant is alive or dead) is being measured, publicly available information should be used to determine vital status only as appropriately directed in accordance with local law.

7.3. Lost to Follow-Up

A participant will be considered lost to follow-up if the participant repeatedly fails to return for scheduled visits and the participant's parent(s)/legal guardian is unable to be contacted by the study site.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site must attempt to contact the participant's parent(s)/legal guardian and reschedule the missed visit as soon as possible. Counsel the participant's parent(s) or legal guardian on the importance of maintaining the assigned visit schedule, and ascertain whether the participant's parent(s)/guardian wishes for the participant to continue in the study and/or whether the participant should continue in the study;

- Before a participant is deemed lost to follow-up, the investigator or designee must make every effort to regain contact with the participant's parent(s)/legal guardian (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record;

- Should the participant's parent(s)/legal guardian continue to be unreachable, the participant will be considered to have withdrawn from the study.

8. STUDY ASSESSMENTS AND PROCEDURES

8.1. Administrative Procedures

The investigator (or an appropriate delegate at the investigator site) must obtain a signed and dated ICD before performing any study-specific procedures.

The date of birth will be collected to critically evaluate the immune response and safety profile by age.

Study procedures and their timing are summarized in the SoA. Protocol waivers or exemptions are not allowed.

Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Every effort should be made to ensure that protocol-required tests and procedures are completed as described. However, it is anticipated that from time to time there may be circumstances outside the control of the investigator that make it unfeasible to perform the test. In these cases, the investigator must take all steps necessary to ensure the safety and well-being of the participant. When a protocol-required test cannot be performed, the investigator will document the reason for the missed test and any corrective and preventive actions that they have taken to ensure that required processes are adhered to as soon as possible. The study team must be informed of these incidents in a timely manner. For samples being collected and shipped, detailed collection, processing, storage, and shipment instructions and contact information will be provided to the investigator site prior to initiation of the study.

The total blood sampling volume for individual participants in this study is approximately 15 mL.

8.2. Efficacy and/or Immunogenicity Assessments

Blood will be collected before Dose 1 (Visit 1), approximately 1 month after Dose 1 (Visit 2), and approximately 1 month after Dose 2 (Visit 4) to assess immunogenicity.

Immune Responses

Serotype 3 OPA titers and IgG concentrations will be measured in sera collected at Visits 1, 2, and 4.

Sera collected from all participants may be used for additional testing to better understand the immune responses of the candidate being studied in this protocol, to inform the development of other products, and/or for vaccine-related assay work supporting vaccine programs.

Additional Immunogenicity Assessments

Other exploratory immunological assays (eg, antibody validity, differentiation of IgGs) may be performed if additional sera are available.

No cellular assays will be performed.

8.2.1. Biological Samples

Blood samples will be used only for scientific research. Each sample will be labeled with a code so that the laboratory analyst testing the samples will not know the participant's identity, study visit, or study cohort associated with the sample. Samples that remain after performing assays outlined in the protocol may be stored by Pfizer. Unless a time limitation is required by local regulations or ethical requirements, the samples will be stored for up to 15 years after the end of the study and then destroyed. If allowed by the ICD, stored samples may be used for additional testing to better understand the immune responses to the vaccine(s) under study in this protocol, to inform the development of other vaccines or vaccine-related products, and/or for vaccine-related assay work supporting vaccine programs.

No testing of the participant's genetic material will be performed.

The participant's parent(s)/legal guardian may request that the participant's samples, if still identifiable, be destroyed at any time; however, any data already collected from those samples will still be used for this research. The biological samples may be shared with other researchers as long as confidentiality is maintained, and no testing of the participant's genetic material is performed.

8.3. Safety Assessments

Planned time points for all safety assessments are provided in the SoA. Unscheduled safety measurements may be obtained at any time during the study to assess any perceived safety issues.

8.3.1. Clinical Assessment

A clinical assessment, including medical and vaccine history, will be performed on all participants prior to receipt of study intervention administration at Visit 1 to determine participant eligibility and to establish a clinical baseline. Significant medical history and significant findings from any physical examination (if performed) will be recorded as medical history in the CRF.

Investigators should pay special attention to clinical signs related to previous serious illnesses.

Physical examination findings collected during the study will be considered source record and will not be required to be reported, unless otherwise noted. Any untoward physical examination findings that are identified during the active collection period and meet the definition of an AE or SAE (Appendix 2) must be reported according to the processes in Sections 8.4.1 to 8.4.3.

8.3.1.1. Temperature

Body temperature measured as appropriate for age will be assessed at each visit when study intervention will be administered.

Any untoward temperature findings that are identified during the active collection period and meet the definition of an AE or SAE (Appendix 2) must be reported according to the processes in Sections 8.4.1 to 8.4.3.

8.3.1.2. Postinjection Observation

The participant will be observed for 30 minutes after each dose, and any reactions occurring during that time will be recorded as AEs.

8.3.2. Clinical Safety Laboratory Assessments

Clinical safety laboratory assessments will not be collected in this study.

8.3.3. Participant Electronic Diary

Participants' parent(s)/legal guardians will be asked to monitor and record local reactions and systemic events after study intervention administration (Day 1 through Day 7, where Day 1 is the day of study intervention administration) using an e-diary through an application installed on a provisioned device or on the participant's parent(s)/legal guardian's own personal device. This allows recording of these assessments only within a fixed time window, thus providing the accurate representation of the participant's experience. Data reported in the e-diary will be transferred electronically to the e-diary vendor, where they will be available for review by investigators, their appropriately qualified designees, and sponsor staff at all times via an internet-based portal. At intervals agreed to by the vendor and Pfizer, these data will be transferred electronically to Pfizer for analysis and reporting.

The daily e-diary data will not be captured in the CRF. However, if a participant is withdrawn because of prompted events reported in the e-diary, the event(s) should be recorded on the AE page of the CRF, regardless of whether the investigator considers the event(s) to be clinically significant.

The investigator or designee must obtain stop dates for any local reactions and specific systemic events that were ongoing on the last day that the e-diary was completed. The stop dates should be entered in the CRF.

Investigators (or an appropriately qualified designee) are required to review the e-diary data online at frequent intervals (daily is optimal) to evaluate participant compliance and reported events as part of the ongoing safety review.

8.3.3.1. Grading Scale for Prompted Events

The grading scales used in this study to assess prompted events as described below are based on concepts outlined in the FDA CBER guidelines on toxicity grading scales for healthy adults and adolescent volunteers enrolled in preventive vaccine clinical trials,[18] but have been adapted for applicability to healthy infants.

8.3.3.1.1. Local Reactions

For the first 7 days following each dose from Day 1 through Day 7, where Day 1 is the day of study intervention administration, the participant's parent(s)/legal guardian will be asked to assess redness, swelling, and pain at the study intervention injection site (left anterolateral thigh) and to record the symptoms in the e-diary in the evening. Redness and swelling will be measured and recorded in measuring device (caliper) units (range: 1 to >14; an entry in the e-diary of 15 will denote >14), and then categorized during analysis as mild, moderate, or severe based on the grading scale in Table 1. Measuring device units can be converted to centimeters according to the following scale: 1 measuring device unit = 0.5 cm. Pain at the vaccine injection site will be assessed by the participant's parent(s)/legal guardian as mild, moderate, or severe according to the grading scale in Table 1. The participant's parent(s)/legal guardian will be prompted to contact the investigator if the participant experiences a severe (Grade 3) or above local reaction to assess the reaction and perform an unscheduled assessment or visit as appropriate.

Only an investigator is able to classify a participant's local reaction as Grade 4, after physical examination of the participant or documentation from another medically qualified source (eg, emergency room or hospital record). If a participant experiences a Grade 4 local reaction, the investigator must immediately notify the sponsor. Site staff will educate the participant's parent(s)/legal guardian regarding signs and symptoms that would prompt site contact.

The procedure for notification of the sponsor is provided in the ISF or equivalent.

Table 1. Grading Scales for Local Reactions

	Mild Grade 1	Moderate Grade 2	Severe Grade 3[a]	Grade 4[b]
Redness	1 to 4 measuring device units = >0 to 2.0 cm	5 to 14 caliper units (or measuring device units) = >2.0 to 7.0 cm	>14 caliper units (or measuring device units) = >7 cm	Necrosis or exfoliative dermatitis
Swelling	1 to 4 measuring device units = >0 to 2.0 cm	5 to 14 caliper units (or measuring device units) = >2.0 to 7.0 cm	>14 caliper units (or measuring device units) = >7 cm	Necrosis
Pain at injection site (tenderness)	Hurts if gently touched (eg, whimpers, winces, protests, or withdraws)	Hurts if gently touched, with crying	Causes limitation of limb movement	Emergency room visit or hospitalization for severe injection site pain (tenderness) at injection site

Note: If the size of the redness and/or swelling falls between 2 measuring device units, the higher measuring device unit number will be recorded in the e-diary.

a. Parents/legal guardians of participants experiencing Grade 3 local reactions are required to contact the investigator site. In the event that the participant's parent(s)/legal guardian does not call, the investigator will call the participant's parent(s)/legal guardian. An unscheduled visit may be required.
b. Grade 4 assessment should be made by the investigator; Grade 4 local reactions will not be collected in the e-diary but will be collected as AEs on the CRF. The intensity of the local reaction should be graded using the AE intensity grading scale in Section 10.2.3.

8.3.3.1.2. Systemic Events – Symptoms and Fever

8.3.3.1.2.1. Symptoms

For the first 7 days following each dose from Day 1 through Day 7, where Day 1 is the day of study intervention administration, the participant's parent(s)/legal guardian will be asked to assess decreased appetite, drowsiness/increased sleep, and irritability and to record the symptoms in the e-diary (in a provisioned device or application on a personal device) in the evening. The symptoms will be assessed by the participant's parent(s)/legal guardian as mild, moderate, or severe according to the grading scale in Table 2.

The participant's parent(s)/legal guardian will also be instructed to contact site staff if the participant experiences any possible Grade 4 prompted systemic event (ie, emergency room visit or hospitalization for severe decreased appetite, severe drowsiness/increased sleep, or severe irritability) within 7 days after dose administration. Study staff may also contact the participant's parent(s)/legal guardian to obtain additional information on Grade 3 events entered into the e-diary.

Only an investigator is able to classify a participant's systemic event as Grade 4, after physical examination of the participant or documentation from another medically qualified source (eg, emergency room or hospital record) or telephone contact with the participant's parent(s)/legal guardian. If a participant experiences a Grade 4 systemic event, the investigator must immediately notify the sponsor.

The procedure for notification of the sponsor is provided in the ISF or equivalent.

Table 2. Grading Scales for Systemic Events

	Mild Grade 1	Moderate Grade 2	Severe Grade 3	Grade 4[a]
Decreased appetite (loss of appetite)	Decreased interest in eating	Decreased oral intake	Refusal to feed	Emergency room visit or hospitalization for severe decreased appetite (loss of appetite)
Drowsiness (increased sleep)	Increased or prolonged sleeping bouts	Slightly subdued, interfering with daily activity	Disabling, not interested in usual daily activity	Emergency room visit or hospitalization for severe drowsiness (increased sleep)
Irritability (fussiness) (synonymous with restless sleep; decreased sleep)	Easily consolable	Requiring increased attention	Inconsolable; crying cannot be comforted	Emergency room visit or hospitalization for severe irritability (fussiness)

a. Grade 4 assessment should be made by the investigator; Grade 4 systemic events will not be collected in the e-diary but will be collected as AEs on the CRF. The intensity of the systemic event should be graded using the AE intensity grading scale in Section 10.2.3.

8.3.3.1.2.2. Fever

In order to record information on fever, a digital thermometer will be given to the participant's parent(s)/legal guardian with instructions on how to measure axillary temperature at home. Temperature will be collected in the evening, daily, for 7 days following each dose (Days 1 through 7, where Day 1 is the day of study intervention administration) and at any time during the 7 days that fever is suspected. Fever is defined as a temperature of ≥38.0°C (≥100.4°F). The highest temperature for each day will be recorded in the e-diary. In the event of a fever on Day 7, temperature will be collected daily until fever has resolved (1 day of temperature less than 38.0°C [100.4°F]) in order to collect a stop date in the CRF.

A participant's parent(s)/legal guardian will be prompted to contact the investigator if the participant experiences a temperature >40.0°C (>104.0°F) to assess the fever and perform an unscheduled assessment, as applicable (see unscheduled assessments in Section 8.10.5). Study staff may also contact the participant's parent(s)/legal guardian to obtain additional information if a temperature of >38.9°C (>102.0°F) is entered into an e-diary. Temperature will be measured and recorded to 1 decimal place and then grouped into ranges for the analysis; see Table 3.

Table 3. Ranges for Fever

≥38.0°C to 38.4°C
>38.4°C to 38.9°C
>38.9°C to 40.0°C[a]
>40.0°C[a]

Note: Fever is defined as a temperature of ≥38.0°C.

a. Participants reporting a fever >104.0°F (>40.0°C) will be prompted to contact the study site.

8.3.3.1.3. Use of Antipyretic/Pain Medication

The participant's parent(s)/legal guardian will be asked to record the use of antipyretic/pain medication (yes/no) in the e-diary (in a provisioned device or application on a personal device) in the evening, daily, for 7 days after each dose of study intervention. The use of prophylactic antipyretic/pain medication, while permitted, is not recommended on the day of study intervention administration (before or after study intervention administration). If symptoms develop, the use of antipyretic/pain medication is allowed.

8.4. Adverse Events, Serious Adverse Events, and Other Safety Reporting

The definitions of an AE and an SAE can be found in Appendix 2.

AEs may arise from symptoms or other complaints reported to the investigator by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative), or they may arise from clinical findings of the investigator or other healthcare providers (clinical signs, test results, etc).

The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible to pursue and obtain adequate information both to determine the outcome and to assess whether the event meets the criteria for classification as an SAE or caused the participant to discontinue the study intervention (see Section 7.1).

During the active collection period as described in Section 8.4.1, each participant's parent(s)/legal guardian will be questioned about the occurrence of AEs in a nonleading manner.

In addition, the investigator may be requested by Pfizer Safety to obtain specific follow-up information in an expedited fashion.

8.4.1. Time Period and Frequency for Collecting AE and SAE Information

The time period for actively eliciting and collecting AEs and SAEs ("active collection period") for each participant begins from the time the participant's parent(s)/legal guardian provides informed consent, which is obtained before the participant's participation in the study (ie, before undergoing any study-related procedure and/or receiving study intervention), through and including Visit 4.

Follow-up by the investigator continues throughout the active collection period and until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator.

When a clinically important AE remains ongoing at the end of the active collection period, follow-up by the investigator continues until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator and Pfizer concurs with that assessment.

For participants who are screen failures, the active collection period ends when screen failure status is determined.

If the participant withdraws from the study and also withdraws consent for the collection of future information, the active collection period ends when consent is withdrawn.

If a participant permanently discontinues or temporarily discontinues study intervention because of an AE or SAE, the AE or SAE must be recorded on the CRF and the SAE reported via the PSSA.

Investigators are not obligated to actively seek information on AEs or SAEs after the participant has concluded study participation. However, if the investigator learns of any SAE, including a death, at any time after a participant has completed the study, and they consider the event to be reasonably related to the study intervention, the investigator must promptly report the SAE to Pfizer via the PSSA.

8.4.1.1. Reporting SAEs to Pfizer Safety

All SAEs occurring in a participant during the active collection period as described in Section 8.4.1 are reported to Pfizer Safety via the PSSA immediately upon awareness and under no circumstance should this exceed 24 hours, as indicated in Appendix 2. The investigator will submit any updated SAE data to the sponsor within 24 hours of its being available.

8.4.1.2. Recording Nonserious AEs and SAEs on the CRF

All nonserious AEs and SAEs occurring in a participant during the active collection period, which begins after obtaining informed consent as described in Section 8.4.1, will be recorded on the AE section of the CRF.

The investigator is to record on the CRF all directly observed and all spontaneously reported AEs and SAEs reported by the participant.

As part of ongoing safety reviews conducted by the sponsor, any nonserious AE that is determined by the sponsor to be serious will be reported by the sponsor as an SAE. To assist in the determination of case seriousness, further information may be requested from the investigator to provide clarity and understanding of the event in the context of the clinical study.

8.4.2. Method of Detecting AEs and SAEs

The method of recording, evaluating, and assessing causality of AEs and SAEs and the procedures for completing and transmitting SAE reports are provided in Appendix 2.

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the participant's parent(s)/legal guardian is the preferred method to inquire about AE occurrences.

8.4.3. Follow-Up of AEs and SAEs

After the initial AE or SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. For each event, the investigator must pursue and obtain adequate information until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).

In general, follow-up information will include a description of the event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Any information relevant to the event, such as concomitant medications and illnesses, must be provided. In the case of a participant death, a summary of available autopsy findings must be submitted as soon as possible to Pfizer Safety.

Further information on follow-up procedures is provided in Appendix 2.

8.4.4. Regulatory Reporting Requirements for SAEs

Prompt notification by the investigator to the sponsor of an SAE is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a study intervention under clinical investigation are met.

The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRBs/ECs, and investigators.

Investigator safety reports must be prepared for SUSARs according to local regulatory requirements and sponsor policy and forwarded to investigators as necessary.

An investigator who receives SUSARs or other specific safety information (eg, summary or listing of SAEs) from the sponsor will review and then file it along with the SRSD(s) for the study and will notify the IRB/EC, if appropriate according to local requirements.

8.4.5. Environmental Exposure, Exposure During Pregnancy or Breastfeeding, and Occupational Exposure

Environmental exposure occurs when a person not enrolled in the study as a participant receives unplanned direct contact with or exposure to the study intervention. Such exposure may or may not lead to the occurrence of an AE or SAE. Persons at risk for environmental exposure include healthcare providers, family members, and others who may be exposed. An environmental exposure may include EDP, EDB, and occupational exposure.

Any such exposures to the study intervention under study are reportable to Pfizer Safety within 24 hours of investigator awareness.

8.4.5.1. Exposure During Pregnancy

An EDP occurs if:

- A female nonparticipant is found to be pregnant while being exposed or having been exposed to study intervention because of environmental exposure. Below are examples of environmental EDP:
    - A female family member or healthcare provider reports that she is pregnant after having been exposed to the study intervention by injection, inhalation, or skin contact.
    - A male family member or healthcare provider who has been exposed to the study intervention by injection, inhalation, or skin contact then inseminates his female partner prior to or around the time of conception.

The investigator must report EDP to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The initial information submitted should include the anticipated date of delivery (see below for information related to termination of pregnancy).

- If EDP occurs in the setting of environmental exposure, the investigator must report information to Pfizer Safety via the PSSA. Since the exposure information does not pertain to the participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed report is maintained in the ISF.

- Follow-up is conducted to obtain general information on the pregnancy and its outcome for all EDP reports with an unknown outcome. The investigator will follow the pregnancy until completion (or until pregnancy termination) and notify Pfizer Safety of the outcome as a follow-up to the initial report. In the case of a live birth, the structural integrity of the neonate can be assessed at the time of birth. In the event of a termination, the reason(s) for termination should be specified and, if clinically possible, the structural integrity of the terminated fetus should be assessed by gross visual inspection (unless preprocedure test findings are conclusive for a congenital anomaly and the findings are reported).

Abnormal pregnancy outcomes are considered SAEs. If the outcome of the pregnancy meets the criteria for an SAE (ie, ectopic pregnancy, spontaneous abortion, intrauterine fetal demise, neonatal death, or congenital anomaly in a live-born baby, a terminated fetus, an intrauterine fetal demise, or a neonatal death), the investigator should follow the procedures for reporting SAEs. Additional information about pregnancy outcomes that are reported to Pfizer Safety as SAEs follows:

- Spontaneous abortion, including miscarriage and missed abortion, should be reported as an SAE;

- Neonatal deaths that occur within 1 month of birth should be reported, without regard to causality, as SAEs. In addition, infant deaths after 1 month should be reported as SAEs when the investigator assesses the infant death as related or possibly related to exposure to the study intervention.

Additional information regarding the EDP may be requested by the sponsor. Further follow-up of birth outcomes will be handled on a case-by-case basis (eg, follow-up on preterm infants to identify developmental delays). In the case of paternal exposure, the investigator will provide the participant with the Pregnant Partner Release of Information Form to deliver to his partner. The investigator must document in the source documents that the participant was given the Pregnant Partner Release of Information Form to provide to his partner.

8.4.5.2. Exposure During Breastfeeding

An EDB occurs if:

- A female nonparticipant is found to be breastfeeding while being exposed or having been exposed to study intervention (ie, environmental exposure). An example of environmental EDB is a female family member or healthcare provider who reports that she is breastfeeding after having been exposed to the study intervention by injection, inhalation, or skin contact.

The investigator must report EDB to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The information must be reported via the PSSA. When EDB occurs in the setting of environmental exposure, the exposure information does not pertain to the participant enrolled in the study, so the information is not recorded on a CRF. However, a copy of the completed report is maintained in the ISF.

An EDB report is not created when a Pfizer drug specifically approved for use in breastfeeding women (eg, vitamins) is administered in accordance with authorized use. However, if the infant experiences an SAE associated with such a drug, the SAE is reported together with the EDB.

8.4.5.3. Occupational Exposure

The investigator must report any instance of occupational exposure to Pfizer Safety within 24 hours of the investigator's awareness via the PSSA, regardless of whether there is an associated SAE. Since the information about the occupational exposure does not pertain to a participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed report is maintained in the ISF.

8.4.6. Cardiovascular and Death Events

Not applicable.

8.4.7. Disease-Related Events and/or Disease-Related Outcomes Not Qualifying as AEs or SAEs

Not applicable.

8.4.8. Adverse Events of Special Interest

Not applicable.

8.4.8.1. Lack of Efficacy

The investigator must report signs, symptoms, and/or clinical sequelae resulting from lack of efficacy. Lack of efficacy or failure of expected pharmacological action is reportable to Pfizer Safety only if associated with an SAE.

8.4.9. Medical Device Deficiencies

Medical devices being provided for use in this study are those listed in Section 6.1.2. In order to fulfill regulatory reporting obligations worldwide, the investigator is responsible for the detection and documentation of events meeting the definitions of device deficiency that occur during the study with such devices.

The definition of a medical device deficiency can be found in Appendix 5.

Note: AEs and/or SAEs that are associated with a medical device deficiency will follow the same processes as other AEs or SAEs, as outlined in Sections 8.4.1 through 8.4.4 and Appendix 2 of the protocol.

8.4.9.1. Time Period for Detecting Medical Device Deficiencies

Medical device deficiencies that result in an incident will be detected, documented, and reported during all periods of the study in which the medical device is used.

Importantly, reportable device deficiencies are not limited to problems with the device itself but also include incorrect or improper use of the device and even intentional misuse, etc.

If the investigator learns of any device deficiency at any time after a participant has been discharged from the study, and such deficiency is considered reasonably related to a medical device provided for the study, the investigator will promptly notify the sponsor.

The method of documenting medical device deficiencies is provided in Appendix 5.

8.4.9.2. Follow-Up of Medical Device Deficiencies

Follow-up applies to all participants, including those who discontinue study intervention.

The investigator is responsible for ensuring that follow-up includes any supplemental investigations as indicated to elucidate the nature and/or causality of the deficiency.

New or updated information will be recorded on a follow-up form with all changes signed and dated by the investigator.

8.4.9.3. Prompt Reporting of Device Deficiencies to the Sponsor

When a device deficiency occurs:

1. The investigator notifies the sponsor by telephone or email within 1 business day of determining that the incident meets the protocol definition of a medical device deficiency.

2. The device deficiency must be recorded on the Medical Device Complaint form along with any associated AE (either serious or nonserious) when applicable.

3. If an AE (either serious or nonserious) associated with the device deficiency occurs, then the AE must be entered into the AE section of the CRF.

4. If an SAE associated with the device deficiency is brought to the attention of the investigator, the investigator must immediately notify Pfizer Safety of the SAE (see Section 8.4.1.1). All relevant details related to the role of the device in the event must be reported via the PSSA as outlined in Sections 8.4.1.1 and 8.4.1.2. The same SAE information must be provided on the Medical Device Complaint form.

The sponsor will be the contact for the receipt of device deficiency information.

8.4.9.4. Regulatory Reporting Requirements for Device Deficiencies

The investigator will promptly report all device deficiencies occurring with any medical device provided for use in the study in order for the sponsor to fulfill the legal responsibility to notify appropriate regulatory authorities and other entities about certain safety information relating to medical devices being used in clinical studies.

The investigator, or responsible person according to local requirements (eg, the head of the medical institution), will comply with the applicable local regulatory requirements relating to the reporting of device deficiencies to the IRB/EC.

8.4.10. Vaccination Errors

Vaccination errors may result from the administration or consumption of the study intervention by the wrong participant, or at the wrong time, or at the wrong dosage strength.

Vaccination errors are recorded and reported as follows:

Recorded on the Vaccination Error Page of the CRF	Recorded on the Adverse Event Page of the CRF	Reported on the PSSA to Pfizer Safety Within 24 Hours of Awareness
All vaccination errors (regardless of whether associated with an AE)	Any AE or SAE associated with the vaccination error	Only if associated with an SAE

Vaccination errors include:

- Vaccination errors involving participant exposure to the study intervention;
- Potential vaccination errors or uses outside of what is foreseen in the protocol that do or do not involve the study participant.

Other examples include, but are not limited to:

- The administration of expired study intervention;
- The administration of an incorrect study intervention;
- The administration of an incorrect dosage;
- The administration of study intervention that has undergone temperature excursion from the specified storage range, unless it is determined by the sponsor that the study intervention under question is acceptable for use.

Whether or not the vaccination error is accompanied by an AE, as determined by the investigator, such vaccination errors occurring to a study participant are recorded on the vaccination error page of the CRF, which is a specific version of the AE page, and, if applicable, any associated serious and nonserious AE(s) are recorded on the AE page of the CRF.

In the event of a vaccination dosing error, the sponsor should be notified within 24 hours. Vaccination errors should be reported to Pfizer Safety within 24 hours via the PSSA only when associated with an SAE.

8.5. Pharmacokinetics

Pharmacokinetic parameters are not evaluated in this study.

8.6. Genetics

8.6.1. Specified Genetics

Specified genetic analyses are not evaluated in this study.

8.6.2. Retained Research Samples for Genetics

Not applicable.

8.7. Biomarkers

Biomarkers are not evaluated in this study.

8.8. Immunogenicity Assessments

Immunogenicity assessments are described in Section 8.2.

8.9. Health Economics

Health economics/medical resource utilization and health economics parameters are not evaluated in this study.

8.10. Study Procedures

Before enrollment and before any study-related procedures are performed, voluntary, written, study-specific informed consent will be obtained from the participant's parent(s)/legal guardian. Each signature on the ICD must be personally dated by the signatory. The investigator or their designee will also sign the ICD. A copy of the signed and dated ICD must be given to the participant's parent(s)/legal guardian. The source data must reflect that the informed consent was obtained before participation in the study.

The timing of visit procedures (ie, prior to randomization and after randomization) must be maintained; however, there is flexibility in the order in which the procedures can be conducted at each visit. The ICD must be signed prior to the start of any study procedure.

8.10.1. Visit 1 – Dose 1 (Day 1)

Prior to randomization:

- Obtain a personally signed and dated ICD indicating that the participant's parent(s)/legal guardian has been informed of all pertinent aspects of the study before performing any study-specific procedures.
- Assign a participant number via the IRT.
- Obtain and record the participant's demographic information (including date of birth, sex, race, and ethnicity). The complete date of birth (ie, DD-MMM-YYYY) will be collected to critically evaluate the immune response and safety profile by age.
- Perform a clinical assessment. If the clinical assessment indicates that a physical examination is necessary to comprehensively evaluate the participant, perform a physical examination and record any findings in the source documents and, if significant, record such findings on the medical history CRF.
- Measure and record the participant's prevaccination body temperature using a method appropriate for the age of the toddler, according to routine local practice (°C).
- Record receipt of 2 infant doses of PCV10 (prior to 11 months of age), including dates given.
- Record nonstudy vaccinations given up to 28 days prior to study intervention administration, in source documents and in the CRF, if applicable. (Refer to Section 6.9 for acceptable concomitant vaccines and prohibited vaccines.)
- Ensure and document that all of the inclusion criteria and none of the exclusion criteria are met.
- Assign a randomization number and a study intervention container number via the IRT. This must be the last step before proceeding. A site staff member will prepare the study intervention according to the IPM.

After randomization:

- Review temporary delay criteria.
- Collect approximately 5 mL of blood prior to study intervention administration.
- Administer a single 0.5-mL injection of the assigned study intervention into the left anterolateral thigh (see Section 8.1).
- Administer the third (toddler) dose of PCV10 into the right anterolateral thigh (see Section 8.1).
- If allowed, administer routine pediatric vaccinations into a limb other than the site of study intervention (mPnC candidate or mPnC control) injection and capture all details of concomitant vaccine given on the same day as study intervention, including the name, date of administration, and site of administration, on the CRF (see Section 6.9).

After study intervention administration:

- Site staff will observe the participant for 30 minutes after administration of study intervention for any reactions. Record any acute reactions (including time of onset) in the participant's source documents and on the AE page of the CRF, and via the PSSA, as applicable.
- Record concomitant medications used to treat SAEs, if applicable.
- Record AEs and SAEs as described in Section 8.4.
- Explain the e-diary technologies available for this study (Section 8.3.3) and assist the participant's parent(s)/legal guardian in downloading the study application onto the participant's parent(s)/legal guardian's own device or issue a provisioned device, if required. Provide instructions on the e-diary's use and completion and ask the participant's parent(s)/legal guardian to complete the e-diary from Day 1 through Day 7, with Day 1 being the day of study intervention administration.
- Issue the participant's parent(s)/legal guardian a measuring device to measure injection site reactions and a digital thermometer and provide instructions on their use.
- Ask the participant's parent(s)/legal guardian to contact the investigator site staff or investigator as soon as possible during the 7-day postadministration period if the participant has redness and/or swelling at the injection site measuring >14 measuring device units (>7 cm) or severe injection site pain (causes limitation of limb movement) to determine if an unscheduled visit is required (refer to Section 8.10.5).

- Ask the participant's parent(s) or legal guardian to contact the investigator site staff or investigator as soon as possible if the participant experiences a fever ≥104°F (≥40.0°C) from Day 1 through Day 7 after study intervention administration (where Day 1 is the day of administration) to determine if an unscheduled visit is required (see Section 8.10.5).

- Ask the participant's parent(s)/legal guardian to contact the site staff or investigator immediately if any significant illness or medical event (eg, emergency room visit or hospitalization) occurs to the participant.

- Provide the participant's parent(s)/legal guardian with the participant contact card containing the study and investigator information.

- Inform the participant's parent(s)/legal guardian that the use of prophylactic antipyretic/pain medication, while permitted, is not recommended on the day of study intervention administration (before or after study intervention administration). If symptoms develop, the use of antipyretic/pain medication is allowed.

- Schedule an appointment for the participant to return for the next study visit.

- The investigator or an authorized designee completes the CRF and the source documents and updates the study intervention accountability records.

- The investigator or appropriately qualified designee reviews the e-diary data online at frequent intervals (daily is optimal) for the 7 days (Day 1 is the day of study intervention administration) following administration to evaluate participant compliance and as part of the ongoing safety review.

8.10.2. Visit 2 – Dose 1 Follow-Up Visit (28-42 Days After Visit 1)

- Ensure and document that the participant continues to be eligible for the study (see Section 7.1 and Section 7.2 for participant discontinuation/withdrawal).

- Record nonstudy vaccinations since the last visit in the source documents and in the CRF, if applicable, as described in Section 6.9.

- Review the participant's e-diary data. Collect stop dates of any e-diary events (local reactions or systemic events) ongoing on the last day that the e-diary was completed and record stop dates in the CRF.

- Determine if any AEs (including nonserious AEs and SAEs) have occurred since the previous visit, follow up on any previously reported events to determine the outcome (ie, record stop dates or confirm if they are still continuing), and record such AEs as described in Section 8.4.

- Record concomitant medications used to treat SAEs.

- Collect approximately 5 mL of blood for immunogenicity assessments.
- If allowed, administer routine pediatric vaccinations and capture all details of concomitant vaccine(s), including the name, date of administration, and site of administration, on the CRF (see Section 6.9).
- Remind the parent(s)/legal guardian to bring back the e-diary device for the next visit, if applicable.
- Confirm whether the participant's parent(s)/legal guardian still possesses the participant contact card containing the study and investigator information. Provide a participant contact card, if needed.
- Schedule an appointment for the participant to return for the next study visit.
- Remind the participant's parent(s)/legal guardian to contact the investigator or investigator site staff as soon as possible if any significant illness or medical event (eg, emergency room visit or hospitalization) occurs during the study period.
- The investigator or an authorized designee completes the CRF and the source documents.

8.10.3. Visit 3 – Dose 2 (56-70 Days After Visit 1/Dose 1)

- Ensure and document that the participant continues to be eligible for the study (see Section 7.1 and Section 7.2 for participant discontinuation/withdrawal).
- Record nonstudy vaccinations since the last visit, if applicable, as described in Section 6.9.
- If applicable, collect stop dates of any Dose 1 e-diary events (local reactions or systemic events) ongoing on the last day that the Dose 1 e-diary was completed and record stop dates in the CRF.
- Determine if any AEs (including nonserious AEs and SAEs) have occurred since the previous visit, follow up on any previously reported events to determine the outcome (ie, record stop dates or confirm if they are still continuing), and record such AEs as described in Section 8.4.
- Record concomitant medications used to treat SAEs.
- Measure and record the participant's prevaccination body temperature using a method appropriate for the age of the toddler, according to routine local practice (°C).
- Review temporary delay criteria.

- Administer a single 0.5-mL injection of the assigned study intervention into the left anterolateral thigh (see Section 6.1).

- If allowed, administer routine pediatric vaccinations into a limb other than the site of the study intervention injection and capture all details of the concomitant vaccine given on the same day as study intervention administration, including the name, date of administration, and site of administration, on the CRF (see Section 6.9).

After study intervention administration:

- Site staff will observe the participant for 30 minutes after administration of study intervention for any reactions. Record any acute reactions (including time of onset) in the participant's source documents and on the AE page of the CRF, and via the PSSA, as applicable.

- Record concomitant medications used to treat SAEs, if applicable.

- Record AEs and SAEs as described in Section 8.4.

- Assist the participant's parent(s)/legal guardian in redownloading the study application onto the participant's parent(s)/legal guardian's own device or reissue a provisioned device, if required. Provide instructions on the e-diary's use and completion and ask the participant's parent(s)/legal guardian to complete the e-diary from Day 1 through Day 7, with Day 1 being the day of study intervention administration (see Section 8.3.3).

- Confirm if the parent(s)/legal guardian still possesses the measuring device and digital thermometer. Reissue and provide instructions on their use, if needed.

- Ask the participant's parent(s)/legal guardian to contact the investigator site staff or investigator as soon as possible during the 7-day postadministration period if the participant has redness and/or swelling at the injection site measuring >14 measuring device units (>7 cm) or severe injection site pain (causes limitation of limb movement) to determine if an unscheduled visit is required (refer to Section 8.10.5).

- Ask the participant's parent(s)/legal guardian to contact the investigator site staff or investigator as soon as possible if the participant experiences a fever ≥104°F (≥40.0°C) from Day 1 through Day 7 after study intervention administration (where Day 1 is the day of administration) to determine if an unscheduled visit is required (see Section 8.10.5).

- Ask the participant's parent(s)/legal guardian to contact the site staff or investigator immediately if any significant illness or medical event (eg, emergency room visit or hospitalization) occurs to the participant.

- Confirm whether the participant's parent(s)/legal guardian still possesses the participant contact card containing the study and investigator information. Provide a participant contact card, if needed.

- Schedule an appointment for the participant to return for the next study visit.

- The investigator or an authorized designee completes the CRF and the source documents and updates the study intervention accountability records.

- The investigator or appropriately qualified designee reviews the e-diary data online at frequent intervals (daily is optimal) for the 7 days (Day 1 is the day of study intervention administration) following administration to evaluate participant compliance and as part of the ongoing safety review.

8.10.4. Visit 4 – Dose 2 Follow-Up Visit (28-42 Days After Visit 3)

- Record nonstudy vaccinations since the last visit, if applicable, as described in Section 6.9.

- Review the participant's e-diary data. Collect stop dates of any e-diary events (local reactions or systemic events) ongoing on the last day that the e-diary was completed and record stop dates in the CRF.

- Determine if any AEs (including nonserious AEs and SAEs) have occurred since the previous visit, follow up on any previously reported events to determine the outcome (ie, record stop dates or confirm if they are still continuing), and record such AEs as described in Section 8.4.

- Collect the e-diary device, if applicable.

- Record concomitant medications used to treat SAEs.

- Collect approximately 5 mL of blood for immunogenicity assessments.

- If allowed, administer routine pediatric vaccinations and capture all details of the concomitant vaccine(s), including the name, date of administration, and site of administration, on the CRF (see Section 6.9).

- The investigator or an authorized designee completes the CRF and the source documents.

8.10.5. Unscheduled Visits

If the participant's parent(s)/legal guardian reports redness or swelling at the injection site measuring >14 measuring device units (>7.0 cm) or severe injection site pain (Section 8.3.3.1.1), or a temperature >40°C (>104.0°F) (Section 8.3.3.1.2.2) during the 7 days following study intervention administration, a telephone contact must occur as soon as possible between the investigator or medically qualified designee and the participant's parent(s)/legal guardian to assess if an unscheduled investigator site visit is required. Note that for a fever >40.0°C, the participant's parent(s)/legal guardian should be instructed not to delay seeking medical care, as appropriate, while arranging for an unscheduled visit if applicable. A site visit should be scheduled as soon as possible to assess the extent of the injection site reaction unless any of the following is true:

- The participant is unable to attend the unscheduled visit.
- The reaction is no longer present at the time of the telephone contact.
- The participant's parent(s)/legal guardian recorded an incorrect value in the e-diary (confirmation of an e-diary data entry error).
- The PI or authorized designee determined it was not needed.

This telephone contact will be recorded in the participant's source documentation and the CRF. If the participant is unable to attend the unscheduled visit, or the PI or authorized designee determined it was not needed, any ongoing reactions must be assessed at the next study visit. During the unscheduled visit, the reactions should be assessed by the investigator or a medically qualified member of the study staff, such as a study physician or a study nurse, as applicable to the investigator's local practice, who will:

- Measure body temperature, as appropriate for the age of the toddler, according to routine local practice (°F/°C).
- Measure minimum and maximum diameters of redness (if present).
- Measure minimum and maximum diameters of swelling (if present).
- Assess injection site pain (if present) in accordance with the grades provided in Section 8.3.3.1.1.
- Assess for other findings associated with the reaction and record on the AE page of the CRF, if appropriate.

The investigator or an authorized designee will complete the unscheduled visit assessment page of the CRF.

The participant's parent(s)/legal guardian will also be instructed to contact investigator site staff if the participant experiences any emergency room visit or hospitalization for decreased appetite, drowsiness/increased sleep, irritability, or local reaction within 7 days after administration of study intervention.

The participant's parent(s)/legal guardian will also be instructed to contact the investigator site to report any significant illness, medical event, or hospitalization that occurs during the study period. The investigator site should determine if an unscheduled visit to further evaluate the event is warranted in all such cases.

Additionally, study staff may contact the participant's parent(s)/legal guardian to obtain additional information on Grade 3 events entered into the e-diary.

9. STATISTICAL CONSIDERATIONS

Methodology for summary and statistical analyses of the data collected in this study is described here and further detailed in the SAP, which will be maintained by the sponsor. The SAP may modify what is outlined in the protocol where appropriate; however, any major modifications of the primary endpoint definitions or their analyses will also be reflected in a protocol amendment.

9.1. Statistical Hypothesis

There is no formal statistical hypothesis testing planned for this study.

9.1.1. Estimands

The estimands corresponding to the primary and secondary objectives are described in the table in Section 3. The estimands to evaluate the immunogenicity objectives will be based on the evaluable immunogenicity populations (see Section 9.2 for definition). The estimands estimate the study intervention effect in the hypothetical setting where participants follow the study schedules and protocol requirements as directed. Missing serology results will not be imputed.

In the safety primary objective evaluations, missing e-diary data will not be imputed. A partial AE start date (eg, missing day, missing both month and day) will be imputed by assigning the earliest possible start date using all available information (eg, stop date of AE, date of study intervention administration from the same participant) following the Pfizer standards for handling incomplete AE start date. An AE with a completely missing start date is not allowed in the data collection. No other missing information will be imputed in the safety analysis.

9.2. Analysis Sets

For purposes of analysis, the following analysis sets are defined:

Participant Analysis Set	Description
Enrolled	All participants whose parents/legal guardians sign the ICD.
Randomized	All participants who are assigned a randomization number in the IRT system.
Dose 1 evaluable immunogenicity	All randomized participants who 1. are eligible, 2. receive the first dose of study intervention to which they are randomly assigned, 3. have at least 1 valid immunogenicity result from the blood sample collected within an appropriate window 1 month after Dose 1, and 4. have no other major protocol deviations as determined by the clinician up to the 1-month post–Dose 1 visit.
Dose 2 evaluable immunogenicity	All randomized participants who 1. are eligible, 2. receive both doses of study intervention to which they are randomly assigned, 3. have at least 1 valid immunogenicity result from the blood sample collected within an appropriate window 1 month after Dose 2, and 4. have no other major protocol deviations as determined by the clinician.
mITT	All randomized participants who receive the study intervention with at least 1 valid immunogenicity result 1 month after Dose 1 and/or 1 month after Dose 2.
Safety	All participants who receive at least 1 dose of study intervention.

9.3. Statistical Analyses

The SAP will be developed and finalized before any of the planned analyses (Section 9.4.1) are performed and will describe the analyses and procedures for accounting for missing, unused, and spurious data. This section is a summary of the planned statistical analyses of the primary and secondary endpoints.

9.3.1. General Considerations

In general, the study data will be summarized by study intervention groups. CIs for all endpoints in the statistical analysis will be presented as 2-sided at the 95% level.

For all the immunogenicity endpoints, the analysis will be primarily based on the evaluable immunogenicity populations. An additional analysis will be performed based on the mITT population if there is a large enough difference in the number of participants included between the mITT and the evaluable immunogenicity populations. Participants will be summarized according to the study intervention group to which they were randomized. Missing laboratory results will not be imputed.

The safety analyses are based on the safety population. Participants will be summarized according to the study interventions they received.

9.3.1.1. Analyses for Binary Data

Descriptive statistics for categorical variables (eg, proportions) are the percentage (%), the numerator (n) and denominator (N) used in the percentage calculation, and the 2-sided 95% CIs, where applicable.

The exact 95% CI for binary endpoints for each group will be computed using the F distribution (Clopper-Pearson).

9.3.1.2. Analyses for Continuous Data

Unless otherwise stated, descriptive statistics for continuous variables are n, mean, median, standard deviation, minimum, and maximum.

Assay results above the LLOQ will be reported, but results that are below the LLOQ, or BLQs, will be set to 0.5 × LLOQ in the calculation of GMCs and set to LLOQ in the analysis of fold rises.

9.3.1.3. Geometric Means

The geometric mean for each group will be calculated as the mean of the logarithmically transformed assay results and then exponentiating the mean. The 2-sided 95% CI will be obtained by exponentiating the CI for the mean of the logarithmically transformed assay results based on the Student t distribution.

9.3.1.4. Geometric Mean Fold Rises

The GMFR for each group is defined as the geometric mean of the fold rises in the assay results from 1 time point to a later time point. Only data from participants with nonmissing assay results at both time points will be included in the GMFR calculation.

The GMFR will be calculated as the mean difference of logarithmically transformed assay results (later time point - earlier time point) and exponentiating the mean difference. The 2-sided 95% CI will be obtained by exponentiating the limits of the CI for the mean difference of the logarithmically transformed assay results based on the Student t distribution.

9.3.1.5. Reverse Cumulative Distribution Curves

Empirical RCDCs for IgG concentrations and OPA titers will be plotted as a step function of the proportion of participants with the assay result equal to or exceeding a specified value over the full range of the observed assay results.

9.3.2. Primary Endpoint(s)/Estimand(s) Analysis

Objectives	Endpoints and Estimands	Statistics
Safety[a]	• Percentage of participants with prompted local reactions (redness, swelling, and pain at the injection site) within 7 days after each dose in each group • Percentage of participants with prompted systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability) within 7 days after each dose in each group	• Descriptive summary statistics for participants with each local reaction/systemic event within 7 days after each dose, by severity level
	• Percentage of participants with AEs from Dose 1 through 1 month after Dose 2	• Descriptive summary statistics
	• Percentage of participants with SAEs from Dose 1 through 1 month after Dose 2	• Descriptive summary statistics

a. Any related AEs starting within 7 days after each dose, and collected by the AE CRF, that are considered local reactions or systemic events will be consolidated with e-diary data and included in the corresponding summary for local reactions or systemic events.

9.3.3. Secondary Endpoint(s)/Estimand(s) Analysis

Objectives	Endpoints and Estimands	Statistics
Immunogenicity	• Pneumococcal IgG GMCs 1 month after Dose 1 and 1 month after Dose 2	• GMCs and 2-sided 95% CIs
	• Percentages of participants with predefined IgG concentrations 1 month after Dose 1 and 1 month after Dose 2	• Descriptive summary statistics

Objectives	Endpoints and Estimands	Statistics
	• Pneumococcal IgG GMFRs from before Dose 1 to 1 month after Dose 1 and from 1 month after Dose 1 to 1 month after Dose 2	• GMFRs and 2-sided 95% CIs
	• Pneumococcal OPA GMTs 1 month after Dose 1 and 1 month after Dose 2	• GMTs and 2-sided 95% CIs
	• Pneumococcal OPA GMFRs from before Dose 1 to 1 month after Dose 1 and from 1 month after Dose 1 to 1 month after Dose 2	• Descriptive summary statistics

9.3.4. Exploratory Endpoint(s) Analysis

The analyses on the exploratory endpoints CCI [redacted] will be provided in the SAP.

9.4. Interim Analyses

No interim analysis will be conducted for this study. As this is an open-label study, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessment and/or for supporting clinical development.

9.4.1. Analysis Timing

Statistical analyses may be carried out as specified below:

- Analysis of safety data through Visit 2 (1 month after Dose 1);
- Analysis of immunogenicity data of IgG and OPA results through Visit 2 (1 month after Dose 1), when available, for 1 or more immunogenicity endpoints;
- Final analysis of safety and immunogenicity, including complete IgG and OPA results available after the completion of the study.

Immunogenicity data reviews by the sponsor may be conducted at any time the data are available to aid in decision-making for the sponsor programs.

Certain analyses may be combined if the data become available around the same time. Additional analyses may be conducted or combined if required for regulatory purposes or for further clinical evaluation of the study intervention.

9.5. Sample Size Determination

The sample size of this study is not driven by any formal hypothesis test. It is determined primarily based on the consideration of providing initial information on the immune responses induced by the mPnC candidate and the corresponding safety profiles in order to support a decision for further clinical development.

The safety primary objective includes the endpoints for AEs, local reactions, and systemic events. Table 4 shows the binomial probability of detecting at least 1 AE. The number of participants in each study group is 50, which provides a >92% chance of observing at least 1 event in a group, assuming a true event rate of at least 5%.

Table 4. Probability of Detecting at Least 1 Adverse Event

Sample Size per Group	True Rate of AEs	Probability of Observing at Least 1 AE
50	2.0%	63.6%
	3.0%	78.2%
	4.0%	87.0%
	5.0%	92.3%
	6.0%	95.5%

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

10.1.1. Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines, including the Declaration of Helsinki and CIOMS International Ethical Guidelines;
- Applicable ICH GCP guidelines;
- Applicable laws and regulations, including applicable privacy laws.

The protocol, protocol amendments, ICD, SRSD(s), and other relevant documents (eg, advertisements) must be reviewed and approved by the sponsor, submitted to an IRB/EC by the investigator, and reviewed and approved by the IRB/EC before the study is initiated.

Any amendments to the protocol will require IRB/EC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

Protocols and any substantial amendments to the protocol will require health authority approval prior to initiation, except for changes necessary to eliminate an immediate hazard to study participants.

The investigator will be responsible for the following:

- Providing written summaries of the status of the study to the IRB/EC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/EC;
- Notifying the IRB/EC of SAEs or other significant safety findings as required by IRB/EC procedures;
- Providing oversight of the conduct of the study at the site and adherence to requirements of 21 CFR, ICH GCP guidelines, the IRB/EC, European regulation 536/2014 for clinical studies, European MDR 2017/745 for clinical device research, and all other applicable local regulations.

10.1.1.1. Reporting of Safety Issues and Serious Breaches of the Protocol or ICH GCP

In the event of any prohibition or restriction imposed (ie, clinical hold) by an applicable regulatory authority in any area of the world, or if the investigator is aware of any new information that might influence the evaluation of the benefits and risks of the study intervention, Pfizer should be informed immediately.

In addition, the investigator will inform Pfizer immediately of any urgent safety measures taken by the investigator to protect the study participants against any immediate hazard, and of any serious breaches of this protocol or of the ICH GCP guidelines that the investigator becomes aware of.

10.1.2. Financial Disclosure

Investigators and subinvestigators will provide the sponsor with sufficient, accurate financial information as requested to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

10.1.3. Informed Consent Process

The investigator or their representative will explain the nature of the study to the participant's parent(s)/legal guardian and answer all questions regarding the study. The participant's parent(s)/legal guardian should be given sufficient time and opportunity to ask questions and to decide whether or not to participate in the trial.

When consent is obtained from a participant's parent(s)/legal guardian, the participant's assent (affirmative agreement) must be subsequently obtained when the participant has the capacity to provide assent, as determined by the IRB/EC. If the investigator determines that a participant's decisional capacity is so limited they cannot reasonably be consulted, then, as permitted by the IRB/EC and consistent with local regulatory and legal requirements, the participant's assent may be waived with source documentation of the reason assent was not obtained. If the study participant does not provide their own assent, the source documents must record why the participant did not provide assent (for example, the child is not of assenting age per local regulations or policies), how the investigator determined that the person signing the consent was the participant's parent(s)/legal guardian, the consent signer's relationship to the study participant, and that the participant's assent was obtained or waived. If assent is obtained verbally, it must be documented in the source documents.

If study participants are minors who reach the age of majority or if a child reaches the age of assent (per local IRB/EC requirements) during the study, as recognized under local law, the child or adolescent must then provide the appropriate assent or consent to document their willingness to continue in the study. For an adolescent who reaches the age of consent, parental consent would no longer be valid. If the enrollment of emancipated minors is permitted by the IRB/EC and local law, the participant must provide documentation of legal status to give consent without the permission of a legally authorized representative.

Participants and their parents/legal guardians must be informed that their participation is voluntary. The participant's parent(s)/legal guardian will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, HIPAA requirements, where applicable, and the IRB/EC or study center.

The investigator must ensure that each study participant's parent(s)/legal guardian is fully informed about the nature and objectives of the study, the sharing of data related to the study, and possible risks associated with participation, including the risks associated with the processing of the participant's personal data.

The participant's parent(s)/legal guardian must be informed that the participant's personal study-related data will be used by the sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant's parent(s)/legal guardian.

The participant's parent(s)/legal guardian must be informed that the participant's medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/EC members, and by inspectors from regulatory authorities.

The investigator further must ensure that each study participant's parent(s)/legal guardian is fully informed about their right to access and correct their child's personal data and to withdraw consent for the processing of their child's personal data, keeping in mind the privacy rights that may restrict access of older adolescents' medical records by their parent(s)/legal guardian in certain regions.

The source documentation must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date the written consent/assent was obtained. The authorized person obtaining the informed consent must also sign the ICD.

The participants' parents/legal guardians must be reconsented to the most current version of the ICD(s) during their participation in the study as required per local regulations.

A copy of the ICD(s), if written, must be provided to the parent(s)/legal guardian and the participant.

10.1.4. Data Protection

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of participant data.

Participants' personal data will be stored at the study site in encrypted electronic and/or paper form and will be password protected or secured in a locked room to ensure that only authorized study staff have access. The study site will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, the study site will be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of participants with regard to the processing of personal data, participants will be assigned a single, participant-specific numerical code. Any participant records or data sets that are transferred to the sponsor will contain the numerical code; participant names will not be transferred. All other identifiable data transferred to the sponsor will be identified by this single, participant-specific code. The study site will maintain a confidential list of participants who participated in the study, linking each participant's numerical code to their actual identity and medical record ID. In case of data transfer, the sponsor will protect the confidentiality of participants' personal data consistent with the clinical study agreement and applicable privacy laws.

Information technology systems used to collect, process, and store study-related data are secured by technical and organizational security measures designed to protect such data against accidental or unlawful loss, alteration, or unauthorized disclosure or access.

The sponsor maintains SOPs on how to respond in the event of unauthorized access, use, or disclosure of sponsor information or systems.

10.1.5. Committees Structure

10.1.5.1. Data Monitoring Committee

This study will not use an EDMC.

10.1.6. Dissemination of Clinical Study Data

Pfizer fulfills its commitment to publicly disclose clinical study results through posting the results of studies on www.clinicaltrials.gov (ClinicalTrials.gov), the EudraCT/CTIS, and/or www.pfizer.com, and other public registries and websites in accordance with applicable local laws/regulations. In addition, Pfizer reports study results outside of the requirements of local laws/regulations pursuant to its SOPs.

In all cases, study results are reported by Pfizer in an objective, accurate, balanced, and complete manner and are reported regardless of the outcome of the study or the country in which the study was conducted.

www.clinicaltrials.gov

Pfizer posts clinical trial results on www.clinicaltrials.gov for Pfizer-sponsored interventional studies (conducted in patients) that evaluate the safety and/or efficacy of a product, regardless of the geographical location in which the study is conducted. These results are submitted for posting in accordance with the format and timelines set forth by US law.

EudraCT/CTIS

Pfizer posts clinical trial results on EudraCT/CTIS for Pfizer-sponsored interventional studies in accordance with the format and timelines set forth by EU requirements.

www.pfizer.com

Pfizer posts CSR synopses and plain-language study results summaries on www.pfizer.com for Pfizer-sponsored interventional studies at the same time the corresponding study results are posted to www.clinicaltrials.gov. CSR synopses will have personally identifiable information anonymized.

Documents within marketing applications

Pfizer complies with applicable local laws/regulations to publish clinical documents included in marketing applications. Clinical documents include summary documents and CSRs including the protocol and protocol amendments, sample CRFs, and SAPs. Clinical documents will have personally identifiable information anonymized.

Data sharing

Pfizer provides researchers secure access to participant-level data or full CSRs for the purposes of "bona-fide scientific research" that contributes to the scientific understanding of the disease, target, or compound class. Pfizer will make data from these trials available 18 months after study completion. Participant-level data will be anonymized in accordance with applicable privacy laws and regulations. CSRs will have personally identifiable information anonymized.

Data requests are considered from qualified researchers with the appropriate competencies to perform the proposed analyses. Research teams must include a biostatistician. Data will not be provided to applicants with significant conflicts of interest, including individuals requesting access for commercial/competitive or legal purposes.

10.1.7. Data Quality Assurance

All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the sponsor or designee electronically (eg, laboratory data). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.

Guidance on completion of CRFs will be provided in the CRF Completion Requirements document.

The investigator must ensure that the CRFs are securely stored at the study site in encrypted electronic and/or paper form and are password protected or secured in a locked room to prevent access by unauthorized third parties.

QTLs are predefined parameters that are monitored during the study. Important deviations from the QTLs and any remedial actions taken will be summarized in the CSR.

The investigator must permit study-related monitoring, audits, IRB/EC review, and regulatory agency inspections and provide direct access to source records and documents. This verification may also occur after study completion. It is important that the investigator(s) and their relevant personnel are available during the monitoring visits and possible audits or inspections and that sufficient time is devoted to the process.

Monitoring details describing strategy, including definition of study-critical data items and processes (eg, risk-based initiatives in operations and quality such as risk management and mitigation strategies and analytical risk-based monitoring), methods, responsibilities, and requirements, including handling of noncompliance issues and monitoring techniques (central, virtual, or on-site monitoring), are provided in the data management plan and monitoring plan maintained and utilized by the sponsor or designee.

The sponsor or designee is responsible for the data management of this study, including quality checking of the data.

Records and documents, including signed ICDs, pertaining to the conduct of this study must be retained by the investigator for 15 years after study completion unless local regulations or institutional policies require a longer retention period. No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor. The investigator must ensure that the records continue to be stored securely for as long as they are maintained.

When participant data are to be deleted, the investigator will ensure that all copies of such data are promptly and irrevocably deleted from all systems.

The investigator(s) will notify the sponsor or its agents immediately of any regulatory inspection notification in relation to the study. Furthermore, the investigator will cooperate with the sponsor or its agents to prepare the investigator site for the inspection and will allow the sponsor or its agent, whenever feasible, to be present during the inspection. The investigator site and investigator will promptly resolve any discrepancies that are identified between the study data and the participant's medical records. The investigator will promptly provide copies of the inspection findings to the sponsor or its agent. Before response submission to the regulatory authorities, the investigator will provide the sponsor or its agents with an opportunity to review and comment on responses to any such findings.

10.1.8. Source Documents

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator site.

Data reported on the CRF or entered in the eCRF that are from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.

Definition of what constitutes a source document and its origin can be found in the Source Document Locator, which is maintained by the sites and can be found in the ISF.

Description of the use of the computerized system is documented in the data management plan, which is maintained by the sponsor.

The investigator must maintain accurate documentation (source record) that supports the information entered in the CRF.

The sponsor or designee will perform monitoring to confirm that data entered into the CRF by authorized site personnel are accurate, complete, and verifiable from source documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP guidelines, and all applicable regulatory requirements.

10.1.9. Use of Medical Records

There may be instances when copies of medical records for certain cases are requested by Pfizer Safety, where ethically and scientifically justified and permitted by local regulations, to ensure participant safety.

Due to the potential for a participant to be reidentified from their medical records, the following actions must be taken when medical records are sent to the sponsor or sponsor designee:

- The investigator or site staff must redact personal information from the medical record. The personal information includes, but is not limited to, the following: participant names or initials, participant dates (eg, birth date, date of hospital admission/discharge, date of death), participant ID numbers (eg, Social Security number, health insurance number, medical record number, hospital/institution identifier), participant location information (eg, street address, city, country, postal code, IP address), and participant contact information (eg, telephone/fax number, email address).

- Each medical record must be transmitted to the sponsor or sponsor designee using systems with technical and organizational security measures to ensure the protection of personal data (eg, Florence is the preferred system if available).

- There may be unplanned situations where the sponsor may request medical records (eg, sharing medical records so that the sponsor can provide study-related advice to the investigator). The medical records should be submitted according to the procedure described above.

10.1.10. Study and Site Start and Closure

The study start date is the date of the first participant's first visit.

The sponsor designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor, including (but not limited to) regulatory authority decision, change in opinion of the IRB/EC, or change in benefit-risk assessment. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time upon notification to the sponsor or designee/CRO if requested to do so by the responsible IRB/EC or if such termination is required to protect the health of study participants.

Reasons for the early closure of a study site by the sponsor may include but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IRB/EC or local health authorities, the sponsor's procedures, or the ICH GCP guidelines;
- Inadequate recruitment of participants by the investigator;
- Discontinuation of further study intervention development.

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, the ECs/IRBs, the regulatory authorities, and any CRO(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

Study termination is also provided for in the clinical study agreement. If there is any conflict between the contract and this protocol, the contract will control as to termination rights.

10.1.11. Publication Policy

For multicenter trials, the primary publication will be a joint publication developed by the investigator and Pfizer reporting the primary endpoint(s) of the study covering all study sites. The investigator agrees to refer to the primary publication in any subsequent publications. Pfizer will not provide any financial compensation for the investigator's participation in the preparation of the primary congress abstract, poster, presentation, or primary manuscript for the study.

Investigators are free to publish individual center results that they deem to be clinically meaningful after publication of the overall results of the study or 12 months after primary completion date or study completion at all sites, whichever occurs first, subject to the other requirements described in this section.

The investigator will provide Pfizer an opportunity to review any proposed publication or any other type of disclosure of the study results (collectively, "publication") before it is submitted or otherwise disclosed and will submit all publications to Pfizer 30 days before submission. If any patent action is required to protect intellectual property rights, the investigator agrees to delay the disclosure for a period not to exceed an additional 60 days upon request from Pfizer. This allows Pfizer to protect proprietary information and to provide comments, and the investigator will, on request, remove any previously undisclosed confidential information before disclosure, except for any study-intervention or Pfizer-related information necessary for the appropriate scientific presentation or understanding of the study results. For joint publications, should there be disagreement regarding interpretation and/or presentation of specific analysis results, resolution of, and responsibility for, such disagreements will be the collective responsibility of all authors of the publication.

For all publications relating to the study, the investigator and Pfizer will comply with recognized ethical standards concerning publications and authorship, including those established by the International Committee of Medical Journal Editors. The investigator will disclose any relationship with Pfizer and any relevant potential conflicts of interest, including any financial or personal relationship with Pfizer, in any publications. All authors will have access to the relevant statistical tables, figures, and reports (in their original format) required to develop the publication.

10.1.12. Sponsor's Medically Qualified Individual

The contact information for the sponsor's MQI for the study is documented in the study contact list located in the supporting study documentation, study portal, or other electronic system.

To facilitate access to their investigator and the sponsor's MQI for study-related medical questions or problems from nonstudy healthcare professionals, participants are provided with an ECC at the time of informed consent. The ECC contains, at a minimum, (a) protocol and study intervention identifiers, (b) participant's study ID number, (c) site emergency phone number active 24 hours/day, 7 days per week, and (d) Pfizer Call Center number.

The ECC is intended to augment, not replace, the established communication pathways between the participant and their investigator and site staff, and between the investigator and sponsor study team. The ECC is only to be used by healthcare professionals not involved in the research study, as a means of reaching the investigator or site staff related to the care of a participant. The Pfizer Call Center number is to be used when the investigator and site staff are unavailable. The Pfizer Call Center number is not for use by the participant directly; if a participant calls that number directly, they will be directed back to the investigator site.

10.2. Appendix 2: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting

10.2.1. Definition of AE

AE Definition
• An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. • Note: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.

Events Meeting the AE Definition
• Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (eg, ECG, radiological scans, vital sign measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. Any abnormal test results that meet any of the conditions below must be recorded as an AE: o Is associated with accompanying symptoms. o Requires additional diagnostic testing or medical/surgical intervention. o Leads to a change in study dosing (outside of any protocol-specified dose adjustments) or discontinuation from the study, significant additional concomitant drug treatment, or other therapy. • Exacerbation of a chronic or intermittent preexisting condition, including an increase in either frequency and/or intensity of the condition. • New condition detected or diagnosed after study intervention administration, even though it may have been present before the start of the study. • Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction. • Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose per se will not be reported as an AE or SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae.

Events NOT Meeting the AE Definition
• Events that, in the clinical judgment of the investigator, are 1) consistent with normal growth and development and 2) do not differ significantly in frequency or severity from expected, are not generally to be considered AEs. Examples may include, but are not limited to, teething, contact diaper rash, spitting up, colic, or typical fussiness/crying in infants and children. • Any clinically significant abnormal laboratory findings or other abnormal safety assessments that are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. • The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the participant's condition. • Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE. • Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital). • Anticipated day-to-day fluctuations of preexisting disease(s) or condition(s) present or detected at the start of the study that do not worsen.

10.2.2. Definition of an SAE

An SAE is defined as any untoward medical occurrence that, at any dose, meets one or more of the criteria listed below:
a. Results in death
b. Is life-threatening • The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe.
c. Requires inpatient hospitalization or prolongation of existing hospitalization • In general, hospitalization signifies that the participant has been admitted (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious.

- Hospitalization for elective treatment of a preexisting condition that did not worsen from baseline is not considered an AE.

d. Results in persistent or significant disability/incapacity

- The term disability means a substantial disruption of a person's ability to conduct normal life functions.
- This definition is not intended to include experiences of relatively minor medical significance, such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle), that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

e. Is a congenital anomaly/birth defect

f. Is a suspected transmission via a Pfizer product of an infectious agent, pathogenic or nonpathogenic

- The event may be suspected from clinical symptoms or laboratory findings indicating an infection in a participant exposed to a Pfizer product. The terms "suspected transmission" and "transmission" are considered synonymous. These cases are considered unexpected and handled as serious expedited cases by pharmacovigilance personnel. Such cases are also considered for reporting as product defects, if appropriate.

g. Other situations:

- Medical or scientific judgment should be exercised by the investigator in deciding whether SAE reporting is appropriate in other situations, such as significant medical events that may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.
- Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

10.2.3. Recording/Reporting and Follow-Up of AEs and/or SAEs During the Active Collection Period

AE and SAE Recording/Reporting

The table below summarizes the requirements for recording AEs on the CRF and for reporting SAEs via the PSSA to Pfizer Safety throughout the active collection period. These requirements are delineated for 3 types of events: (1) SAEs; (2) nonserious AEs; and (3) exposure to the study intervention under study during pregnancy or breastfeeding, and occupational exposure.

It should be noted that the PSSA for reporting of SAE information is not the same as the AE page of the CRF. When the same data are collected, the forms must be completed in a consistent manner. AEs should be recorded using concise medical terminology and the same AE term should be used on both the CRF and the PSSA for reporting of SAE information.

Safety Event	Recorded on the CRF	Reported on the PSSA to Pfizer Safety Within 24 Hours of Awareness
SAE	All	All
Nonserious AE	All	None
Exposure to the study intervention under study during pregnancy or breastfeeding	All AEs or SAEs associated with EDP or EDB Note: Instances of EDP or EDB not associated with an AE or SAE are not captured in the CRF	All instances of EDP are reported (whether or not there is an associated SAE)* All instances of EDB are reported (whether or not there is an associated SAE)**
Environmental or occupational exposure to the product under study to a nonparticipant (not involving EDP or EDB)	None. Exposure to a study nonparticipant is not collected on the CRF	The exposure (whether or not there is an associated AE or SAE) must be reported***

* **EDP** (with or without an associated SAE) is reported to Pfizer Safety via the PSSA.
** **EDB** is reported to Pfizer Safety via the PSSA, which would also include details of any SAE that might be associated with the EDB.
*** **Environmental or occupational exposure:** AEs or SAEs associated with occupational exposure are reported to Pfizer Safety via the PSSA.

- When an AE or SAE occurs, it is the responsibility of the investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostic reports) related to the event.
- The investigator will then record all relevant AE or SAE information in the CRF.
- It is **not** acceptable for the investigator to send photocopies of the participant's medical records to Pfizer Safety in lieu of completion of the PSSA/AE or SAE CRF page.
- There may be instances when copies of medical records for certain cases are requested by Pfizer Safety. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to Pfizer Safety. Refer to Section 10.1.9 for actions that must be taken when medical records are sent to the sponsor or sponsor designee.
- The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE or SAE.

Assessment of Intensity

The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- Mild: A type of AE that is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual ADL.
- Moderate: A type of AE that is usually alleviated with additional specific therapeutic intervention. The event interferes with usual ADL, causing discomfort, but poses no significant or permanent risk of harm to the research participant.
- Severe: A type of AE that interrupts usual ADL, or significantly affects clinical status, or may require intensive therapeutic intervention.

GRADE	If required on the AE page of the CRF, the investigator will use the adjectives MILD, MODERATE, or SEVERE to describe the maximum intensity of the AE. For purposes of consistency, these intensity grades are defined as follows:	
1	MILD	Does not interfere with participant's usual function.
2	MODERATE	Interferes to some extent with participant's usual function.
3	SEVERE	Interferes significantly with participant's usual function.

An event is defined as "serious" when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe.

Assessment of Causality

- The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE or SAE. The investigator will use clinical judgment to determine the relationship.
- A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration, will be considered and investigated.
- The investigator will also consult the IB and/or product information, for marketed products, in their assessment.
- For each AE or SAE, the investigator **must** document in the medical notes that they have reviewed the AE or SAE and have provided an assessment of causality.
- There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report to the sponsor. However, **it is very important that the investigator always make an assessment of causality for every event before the initial transmission of the SAE data to the sponsor.**
- The investigator may change their opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.
- If the investigator does not know whether or not the study intervention caused the event, then the event will be handled as "related to study intervention" for reporting purposes, as defined by the sponsor. In addition, if the investigator determines that an SAE is associated with study procedures, the investigator must record this causal relationship in the source documents and CRF, and report such an assessment in the dedicated section of the PSSA and in accordance with the SAE reporting requirements.

Follow-Up of AEs and SAEs
• The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations, as medically indicated or as requested by the sponsor, to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other healthcare providers. • If a participant dies during participation in the study or during a recognized follow-up period, the investigator will provide Pfizer Safety with a copy of any postmortem findings, including histopathology. • New or updated information will be recorded in the originally submitted documents. • The investigator will submit any updated SAE data to the sponsor within 24 hours of receipt of the information.

10.2.4. Reporting of SAEs

SAE Reporting to Pfizer Safety via an Electronic DCT
• The primary mechanism for reporting an SAE to Pfizer Safety will be the electronic DCT (eg, eSAE or PSSA). • If the electronic system is unavailable, then the site will use the paper SAE report form (see next section) to report the event within 24 hours. • The site will enter the SAE data into the electronic DCT (eg, eSAE or PSSA) or paper form (as applicable) as soon as the data become available. • After the study is completed at a given site, the electronic DCT will be taken off-line to prevent the entry of new data or changes to existing data. • If a site receives a report of a new SAE from a study participant or receives updated data on a previously reported SAE after the electronic DCT has been taken off-line, then the site can report this information on a paper SAE form (see next section) or to Pfizer Safety by telephone.

SAE Reporting to Pfizer Safety via the Vaccine SAE Reporting Form
• Facsimile transmission of the Vaccine SAE Reporting Form is one of the preferred methods to transmit this information to Pfizer Safety. • In circumstances when the facsimile is not working, an alternative method should be used, eg, secured (Transport Layer Security) or password-protected email. If none of these methods can be used, notification by telephone is acceptable with a copy of the Vaccine SAE Reporting Form sent by overnight mail or courier service. • Initial notification via telephone does not replace the need for the investigator to complete and sign the Vaccine SAE Reporting Form pages within the designated reporting time frames.

10.3. Appendix 3: Liver Safety: Suggested Actions and Follow-Up Assessments

Potential Cases of Drug-Induced Liver Injury

Humans exposed to a drug who show no sign of liver injury (as determined by elevations in transaminases) are termed "tolerators," while those who show transient liver injury but adapt are termed "adaptors." In some participants, transaminase elevations are a harbinger of a more serious potential outcome. These participants fail to adapt and therefore are "susceptible" to progressive and serious liver injury, commonly referred to as DILI. Participants who experience a transaminase elevation above 3 × ULN should be monitored more frequently to determine if they are "adaptors" or are "susceptible."

LFTs are not required as a routine safety monitoring procedure in this study. However, should an investigator deem it necessary to assess LFTs because a participant presents with clinical signs/symptoms, such LFT results should be managed and followed as described below.

In the majority of DILI cases, elevations in AST and/or ALT precede T bili elevations (>2 × ULN) by several days or weeks. The increase in T bili typically occurs while AST/ALT is/are still elevated above 3 × ULN (ie, AST/ALT and T bili values will be elevated within the same laboratory sample). In rare instances, by the time T bili elevations are detected, AST/ALT values might have decreased. This occurrence is still regarded as a potential DILI. Therefore, abnormal elevations in either AST OR ALT in addition to T bili that meet the criteria outlined below are considered potential DILI (assessed per Hy's law criteria) cases and should always be considered important medical events, even before all other possible causes of liver injury have been excluded.

The threshold of laboratory abnormalities for a potential DILI case depends on the participant's individual baseline values and underlying conditions. Participants who present with the following laboratory abnormalities should be evaluated further as potential DILI (Hy's law) cases to definitively determine the etiology of the abnormal laboratory values:

- Participants with AST/ALT and T bili baseline values within the normal range who subsequently present with AST OR ALT values ≥3 × ULN AND a T bili value ≥2 × ULN with no evidence of hemolysis and an alkaline phosphatase value <2 × ULN or not available.

- For participants with baseline AST **OR** ALT **OR** T bili values above the ULN, the following threshold values are used in the definition mentioned above, as needed, depending on which values are above the ULN at baseline:

    - Preexisting AST or ALT baseline values above the normal range: AST or ALT values ≥2 times the baseline values AND ≥3 × ULN; or ≥8 × ULN (whichever is smaller).

    - Preexisting values of T bili above the normal range: T bili level increased from baseline value by an amount of ≥1 × ULN **or** if the value reaches ≥3 × ULN (whichever is smaller).

Rises in AST/ALT and T bili separated by more than a few weeks should be assessed individually based on clinical judgment; any case where uncertainty remains as to whether it represents a potential Hy's law case should be reviewed with the sponsor.

The participant should return to the investigator site and be evaluated as soon as possible, preferably within 48 hours from awareness of the abnormal results. This evaluation should include laboratory tests, detailed history, and physical assessment.

In addition to repeating measurements of AST and ALT and T bili for suspected Hy's law cases, additional laboratory tests should include albumin, CK, direct and indirect bilirubin, GGT, PT/INR, eosinophils (%), and alkaline phosphatase. Consideration should also be given to drawing a separate tube of clotted blood and an anticoagulated tube of blood for further testing, as needed, for further contemporaneous analyses at the time of the recognized initial abnormalities to determine etiology. A detailed history, including relevant information, such as review of ethanol, acetaminophen/paracetamol (either by itself or as a coformulated product in prescription or over-the-counter medications), recreational drug, or supplement (herbal) use and consumption, family history, sexual history, travel history, history of contact with a jaundiced person, surgery, blood transfusion, history of liver or allergic disease, and potential occupational exposure to chemicals, should be collected. Further testing for acute hepatitis A, B, C, D, and E infection, total bile acids, liver imaging (eg, biliary tract), and collection of serum samples for acetaminophen/paracetamol drug and/or protein adduct levels may be warranted.

All cases demonstrated on repeat testing as meeting the laboratory criteria of AST/ALT and T bili elevation defined above should be considered potential DILI (Hy's law) cases if no other reason for the LFT abnormalities has yet been found. **Such potential DILI (Hy's law) cases are to be reported as SAEs, irrespective of availability of all the results of the investigations performed to determine etiology of the LFT abnormalities.**

A potential DILI (Hy's law) case becomes a confirmed case only after all results of reasonable investigations have been received and have excluded an alternative etiology.

10.4. Appendix 4: Kidney Safety Monitoring Guidelines

10.4.1. Laboratory Assessment of Change in Kidney Function and Detection of Kidney Injury

Standard kidney safety monitoring requires assessment of baseline and postbaseline Screat measurement to estimate kidney function [Screat-based eGFR] or creatinine clearance [eCrCl]). Baseline and postbaseline Scys makes it feasible to distinguish AKI from other causes of Screat increase. If Screat increase is confirmed after baseline, then reflex measurement of Scys is indicated (for adult and for pediatric participants). Screat and reflex Scys values are needed to estimate the combined Screat-Scys eGFR calculation to ascertain whether eGFR change from baseline is comparable for 2021 CKD-EPI eGFR Screat-only and for 2021 CKD-EPI eGFR combined Screat plus Scys (for adult participants only).

Regardless of whether kidney function monitoring tests are required as a routine safety monitoring procedure in the study, if the investigator or sponsor deems it necessary to further assess kidney safety and quantify kidney function, then these test results should be managed and followed per standard of care.

10.4.2. Age-Specific Kidney Function Calculation Recommendations

10.4.2.1. Infants (1 Month to <2 Years) and Neonates (<1 Month) — Schwartz Equation

eGFR (mL/min/1.73 m^2) = 0.413 × (Ht/Screat)

Ht in cm; Screat in mg/dL.

10.4.3. Adverse Event Grading for Kidney Safety Laboratory Abnormalities

AE grading for decline in kidney function (ie, eGFR or eCrCl) will be according to KDIGO criteria.

10.5. Appendix 5: AEs, ADEs, SAEs, SADEs, USADEs, and Device Deficiencies: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting in Medical Device Studies

Definitions of a Medical Device Deficiency

The definitions and procedures detailed in this appendix are in accordance with ISO 14155 and the European MDR 2017/745 for clinical device research (if applicable).

Both the investigator and the sponsor will comply with all local reporting requirements for medical devices.

The detection and documentation procedures described in this protocol apply to all sponsor medical devices provided for use in the study (see Section 6.1.2 for the list of sponsor medical devices).

10.5.1. Definition of AE and ADE

AE and ADE Definition
• An AE is defined in Appendix 2 (Section 10.2.1). • An ADE is defined as an AE related to the use of an investigational medical device. This definition includes any AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device as well as any event resulting from use error or from intentional misuse of the investigational medical device.

10.5.2. Definition of SAE, SADE, and USADE

SAE Definition
• An SAE is defined in Appendix 2 (Section 10.2.2).
SADE Definition
• An SADE is defined as an ADE that has resulted in any of the consequences characteristic of an SAE. • Any device deficiency that might have led to an SAE if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate.
USADE Definition
• A USADE (also identified as UADE in US Regulation 21 CFR 813.3) is an SADE that by its nature, incidence, severity, or outcome has not been identified in the current version of the risk analysis management file.

10.5.3. Definition of Device Deficiency

Device Deficiency Definition
• A device deficiency is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. Device deficiencies include malfunctions, use errors, and inadequate information supplied by the manufacturer.

10.5.4. Recording/Reporting and Follow-Up of Medical Device Deficiencies

Device Deficiency Recording
• When a device deficiency occurs, it is the responsibility of the investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostic reports) related to the event. • The investigator will then record all relevant device deficiency information in the participant's medical records, in accordance with the investigator's normal clinical practice and will also capture the required information on the Medical Device Complaint form. • It is not acceptable for the investigator to send photocopies of the participant's medical records to Pfizer Safety in lieu of following the reporting process described in the Medical Device Complaint form. • There may be instances when copies of medical records for certain cases are requested by Pfizer Safety. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to Pfizer Safety. Refer to Section 10.1.9 for actions that must be taken when medical records are sent to the sponsor or sponsor designee. • If the investigator determines that the medical device deficiency may have injured the participant (ie, the medical device deficiency is associated with an AE or SAE), then the investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis will be documented in the participant's medical record and recorded as the AE or SAE rather than the individual signs/symptoms. Requirements for recording and reporting an AE or SAE are provided in Appendix 2 (Section 10.2.3). • For device deficiencies, it is very important that the investigator describe any corrective or remedial actions taken to prevent recurrence of the incident. • A remedial action is any action other than routine maintenance or servicing of a medical device where such action is necessary to prevent recurrence of a device deficiency. This includes any amendment to the device design to prevent recurrence.

Assessment of Causality Occurring in Conjunction With a Medical Device Deficiency
• If an AE or SAE has occurred in conjunction with a medical device deficiency, the investigator must assess the relationship between each occurrence of the AE or SAE and the medical device deficiency. The investigator will use clinical judgment to determine the relationship. • A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out. • Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration will be considered and investigated. • The investigator will also consult the IB in their assessment. • For each device deficiency, the investigator **must** document in the medical notes that they have reviewed the device deficiency and have provided an assessment of causality. • There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report to the sponsor. However, it is very important that the investigator always make an assessment of causality for every event before the initial transmission of the SAE data to the sponsor. • The investigator may change their opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment. • The causality assessment is one of the criteria used when determining regulatory reporting requirements.
Follow-Up of Medical Device Deficiency
• The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations, as medically indicated or as requested by the sponsor, to elucidate the nature and/or causality of the device deficiency as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other healthcare providers. • New or updated information regarding the nature of the device deficiency will be recorded in the originally completed Medical Device Complaint form. • New or updated information regarding any SAE that was potentially associated with the medical device deficiency will be submitted to Pfizer Safety via PSSA within 24 hours of receipt of the information, according to the requirements provided in Appendix 2.

10.5.5. Reporting of SAEs

Reporting of an SAE to Pfizer Safety must be performed according to the processes described in Appendix 2 (Section 10.2.4).

10.5.6. Reporting of SADEs

SADE Reporting to Pfizer Safety
Note: There are additional reporting obligations for medical device deficiencies that are potentially related to SAEs (ie, an SADE) that must fulfill the legal responsibility to notify appropriate regulatory authorities and other entities about certain safety information relating to medical devices being used in clinical studies. • Any device deficiency that is associated with an SAE must be reported to the sponsor within 24 hours after the investigator determines that the event meets the definition of a device deficiency. • The sponsor shall review all device deficiencies and determine and document in writing whether they could have led to an SAE. These shall be reported to the regulatory authorities and IRBs/ECs as required by national regulations.

10.6. Appendix 6: Abbreviations

The following is a list of abbreviations that may be used in the protocol.

Abbreviation	Term
7vPnC	7-valent pneumococcal conjugate vaccine
13vPnC	13-valent pneumococcal conjugate vaccine
20vPnC	20-valent pneumococcal conjugate vaccine
ADE	adverse device effect
ADL	activity/activities of daily living
AE	adverse event
AKI	acute kidney injury
$AlPO_4$	aluminum phosphate
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AxMP	auxiliary medicinal product
BLQ	below the limit of quantitation
C5a	complement component 5a
CBER	Center for Biologics Evaluation and Research (United States)
CFR	Code of Federal Regulations (United States)
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
CK	creatine kinase
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	coronavirus disease 2019
CRF	case report form
CCI [redacted]	
CRO	contract research organization
CSR	clinical study report
CT	clinical trial
CTIS	Clinical Trial Information System
DCT	data collection tool
DILI	drug-induced liver injury
DU	dispensable unit
EC	ethics committee
ECC	emergency contact card
ECG	electrocardiogram
eCrCl	estimated creatinine clearance
eCRF	electronic case report form
EDB	exposure during breastfeeding
e-diary	electronic diary
EDMC	external data monitoring committee

Abbreviation	Term
EDP	exposure during pregnancy
eGFR	estimated glomerular filtration rate
EMA	European Medicines Agency
eSAE	electronic serious adverse event
EU	European Union
EudraCT	European Union Drug Regulating Authorities Clinical Trials (European Clinical Trials Database)
FDA	Food and Drug Administration (United States)
GCP	Good Clinical Practice
GGT	gamma-glutamyl transferase
GMC	geometric mean concentration
GMFR	geometric mean fold rise
GMT	geometric mean titer
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
Ht	height
IB	investigator's brochure
ICD	informed consent document
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ID	identification
IgG	immunoglobulin G
IMP	investigational medicinal product
IND	investigational new drug
INR	international normalized ratio
IP	Internet Protocol
IPAL	investigational product accountability log
IPD	invasive pneumococcal disease
IPM	investigational product manual
IRB	institutional review board
IRT	interactive response technology
ISF	investigator site file
ISO	International Organization for Standardization
IWR	interactive Web-based response
KDIGO	Kidney Disease: Improving Global Outcomes
LFT	liver function test
LLOQ	lower limit of quantitation
MDR	medical device regulation
mITT	modified intent-to-treat
mPnC	monovalent pneumococcal conjugate
mPnC3	monovalent pneumococcal serotype 3 conjugate
MQI	medically qualified individual

Abbreviation	Term
N/A	not applicable
NIMP	noninvestigational medicinal product
NIP	national immunization program
OM	otitis media
OPA	opsonophagocytic activity
PCV	pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
PCV15	15-valent pneumococcal conjugate vaccine
PFS	prefilled syringe
PI	principal investigator
PnC3	pneumococcal serotype 3 conjugate
PPE	personal protective equipment
PPSV23	23-valent pneumococcal polysaccharide vaccine
PSSA	Pfizer's Serious Adverse Event Submission Assistant
PT	prothrombin time
QTL	quality tolerance limit
CCI [redacted]	
RCDC	reverse cumulative distribution curve
SADE	serious adverse device effect
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
CCI [redacted]	
Screat	serum creatinine
Scys	serum cystatin C
SmPC	summary of product characteristics
SoA	schedule of activities
SOP	standard operating procedure
SRSD	single reference safety document
SUSAR	suspected unexpected serious adverse reaction
TBD	to be determined
T bili	total bilirubin
UADE	unanticipated adverse device effect
ULN	upper limit of normal
US	United States
USADE	unanticipated serious adverse device effect
VE	vaccine efficacy

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