DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

DMID Protocol Number: 22-0020

Sponsor: Division of Microbiology and Infectious Diseases

STATISTICAL ANALYSIS PLAN

Protocol: NCT05512949 (22-0020A)
Protocol Title: *A Phase 2 Randomized, Open-Label, Multisite Trial to Evaluate the Immunogenicity of Dose Reduction Strategies of the MVA-BN Vaccine*
Version 2.0
DATE: 20 October 2023

NCT05740982 (22-0020B)
Protocol Title: *A Phase 2 Randomized, Open-Label, Multisite Trial to Inform Public Health Strategies Involving the Use of MVA-BN Vaccine for Mpox*
Version 2.0
DATE: 05 August 2024

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 22-0020**
Development Phase:	Phase II
Products:	JYNNEOS Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN)
Form/Route:	Subcutaneous (SC) and Intradermal (ID)
Indication Studied:	Mpox
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	September 7, 2022
Clinical Trial Completion Date:	ongoing
Date of the Analysis Plan:	October 20, 2023
Version Number:	2.0

This study was performed in compliance with Good Clinical Practice.

VERSION HISTORY

SAP Version	Change	Rational
1.0	Not applicable	Original version.
2.0	On page 10, the text "Day 43" was updated to "Day 181" On page 25, the text "Day 43 (i.e., 14 days after the second vaccine for the last participant)" was updated to "Day 181"	Updated to reflect the protocol team's intent to conduct the interim analysis after that timepoint and match other references to this timing in the SAP.

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LIST OF ABBREVIATIONS

AE	Adverse Event
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
C	Celsius
CEF	Chicken Embryo Fibroblast
CFR	Code of Federal Regulations
CI	Confidence Interval
CM	Centimeter
CRF	Case Report Form
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data Safety Monitoring Board
DV	Protocol Deviation
ELISA	Enzyme-linked Immunosorbent Assay
ER	Emergency Room
EUA	Emergency Use Authorization
FA	Functional Scale Assessment
FDA	Food and Drug Administration
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
HIV	Human Immunodeficiency Virus
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	Intradermal
IRB	Institutional Review Board
LOD	Limit of Detection
LLOQ	Lower Limit of Quantification
ULOQ	Upper Limit of Quantification

List of Abbreviations *(continued)*

MAAE	Medically Attended Adverse Event
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
MH	Medical History
mITT	Modified Intention to Treat
mL	Milliliter
mM	Millimolar
MS	Measurement
MOP	Manual of Procedures
MPXV	Monkeypox virus
MVA-BN	JYNNEOS Modified Vaccinia Ankara-Bavarian Nordic
N	Number (typically refers to participants)
NI	Non-inferiority
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
No.	Number
OHRP	Office for Human Research Protections
PI	Principal Investigator
PMID	PubMed reference number
PP	Per Protocol
PRNT	Plaque Reduction Neutralization Test
PT	Preferred Term
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC	Subcutaneous
SDCC	Statistical and Data Coordinating Center
SOC	System Organ Class
SUSAR	Suspected Unexpected Serious Adverse Reactions
$TCID_{50}$	Median Tissue Culture Infectious Dose

List of Abbreviations *(continued)*

TFF	Tangential Flow Filtration
UC	University of California
UP	Unanticipated Problem
U.S.	United States
VV-WR	Vaccinia Virus, Western Reserve Strain
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for Stage 1 of "A Phase 2, Randomized, Open-Label, Multisite Trial to Inform Public Health Strategies Involving the Use of MVA-BN Vaccine for Mpox" (DMID Protocol 22-0020) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the interim and final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA) and ICH. All work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for immunogenicity and safety outcomes, and (4) a list of proposed tables, figures, and listings. Within the table, figure, and listing mock-ups (Appendices 1, 2, and 3), references to CSR sections are included. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

Mpox is a reemerging infectious disease caused by Monkeypox virus (MPXV), a zoonotic orthopoxvirus, primarily transmitted to humans via contact with infected animals, and causing disease similar to smallpox, although with substantially lower mortality [1,2,3]. MPXV is endemic to West and Central Africa, where the incidence of human mpox cases has increased as much as 20-fold since the end of the smallpox vaccination campaign in 1980 [4,5]. Outbreaks in non-endemic countries have been related to the exotic pet trade [6] and international travel [7,8,9]. Prior to the current global mpox outbreak, secondary human-to-human transmission in non-endemic countries was rare [10,11]. On May 18, 2022, the first United States (U.S.) case of mpox was detected as part of the larger global 2022 mpox outbreak. The U.S. was the fourth non-endemic country to detect a case in a returning traveler. On August 4, the U.S. Department of Health and Human Services declared the U.S. mpox outbreak to be a public health emergency.

Vaccination is being used as a mitigation strategy for those exposed to or deemed to be at higher risk of being exposed to mpox. There is one FDA-approved vaccine for mpox: JYNNEOS Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN). A second vaccine, ACAM2000 is likely effective, but is not FDA-approved for mpox and is associated with moderate risk of myocarditis and pericarditis as well as encephalomyelitis, progressive vaccinia, generalized vaccinia, and ocular complications. ACAM2000 should not be given to people with weakened immune systems, eczema, cardiac disease, infants <12 months, or pregnant individuals. Given these attributes of ACAM2000, JYNNEOS is the preferred vaccine during the current outbreak, however there is a limited supply of the vaccine globally with production unlikely to keep up with growing demand. Given this limited supply, dose sparing strategies have been suggested. On August 9, 2022, the U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for a lower (2×10^7) intradermal (ID) dose of JYNNEOS for individuals 18 years of age and older determined to be at high risk for mpox infection.

Several potential dose sparing strategies were considered for this study. Use of a reduced dose administered subcutaneously is unlikely to be of comparable immunogenicity to the licensed subcutaneous (SC) regimen. There were several Phase 1 and 2 trials that evaluated 2-dose regimens of MVA-BN administered SC four weeks apart. Although the 2-dose $5x10^7$ Median Tissue Culture Infectious Dose (TCID50) SC regimen may elicit geometric mean titer (GMT) similar to ACAM2000, the GMT will likely be below that of the licensed 2-dose 1×10^8 MVA-BN regimen. A single 1×10^8 MVA-BN dose has also been suggested for dose sparing, but based on the published literature, it is unlikely to be immunogenically equivalent to the standard licensed 2-dose regimen. The pivotal Phase 3 trial demonstrated that a single dose is likely to provide a significantly lower GMT than the licensed 2-dose MVA-BN regimen. The National Institute of Allergy and Infectious Diseases (NIAID) conducted a Phase 2 trial comparing the standard (now licensed) 2-dose 1×10^8 $TCID_{50}$ MVA-BN SC regimen (liquid formulation) and a 2-dose 2×10^7 $TCID_{50}$ MVA-BN ID regimen (liquid formulation) and found peak vaccinia virus, Western reserve strain (VV-WR) GMT of 49.5 (40.0, 61.3) and 59.6 (48.1, 74.0), respectively [12]. The 2-dose 2×10^7 $TCID_{50}$ ID regimen was non-inferior to the 2-dose 1×10^8 $TCID_{50}$ SC regimen and utilized only one-fifth of the dose. These results are supported by a trial evaluating another MVA vaccine (ACAM3000) which showed ID vaccination at $1x10^7$ $TCID_{50}$ had similar VV-WR GMT to $1x10^8$ $TCID_{50}$ administered SC or IM [13].

This trial is designed to evaluate several unique issues:

- As vaccine supply is not anticipated to meet the demand in the next year, this trial will evaluate dose reduction strategies focused on the ID route, that is, confirming the non-inferiority of the previously studied ID dose ($2x10^7$ $TCID_{50}$) and evaluating one tenth dose of MVA-BN ($1x10^7$ $TCID_{50}$).

- This trial will also assess differences in safety and tolerability of the ID versus the licensed SC regimen as issues of tolerability have been raised by the manufacturer and some in the medical community.

2.1. Purpose of the Analyses

This Statistical Analysis Plan encompasses the interim analysis and final analysis of immunogenicity and safety of two dose sparing strategies including one-fifth ($2x10^7$ $TCID_{50}$) and one-tenth ($1x10^7$ $TCID_{50}$) of the standard dose of MVA-BN (JYNNEOS) administered intradermally (ID) on Day 1 and 29, compared with the standard, licensed regimen of $1x10^8$ $TCID_{50}$ MVA-BN administered subcutaneously (SC) on Day 1 and 29 to be included in the clinical study report. The protocol for DMID 22-0020 calls for a planned interim analysis on the primary endpoint once participants have completed follow-up through Study Day 181 and results are available from the testing lab. The goal of the interim analysis is to inform public health decisions during this global public health crisis. The interim analysis will not be used to inform further conduct of the trial, but data may be disseminated to public health officials and partners as needed and included in publications and presentations to inform the global scientific community.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

Primary

- To determine if peak (Day 43) humoral immune responses following an ID regimen of 2 x 10^7 $TCID_{50}$ MVA-BN are non-inferior to the licensed regimen of 1 x 10^8 $TCID_{50}$ MVA-BN administered SC
- To determine if peak (Day 43) humoral immune responses following an ID regimen of 1 x 10^7 $TCID_{50}$ MVA-BN are non-inferior to the licensed regimen of 1 x 10^8 $TCID_{50}$ MVA-BN administered SC

Secondary

- To determine if individual peak humoral immune responses following each ID regimen are noninferior to the licensed regimen administered SC
- To evaluate humoral immune responses of each ID regimen (separately) compared to licensed SC regimen each study day.
- To evaluate the kinetics of the humoral immune responses of each ID regimen (separately) compared to licensed SC regimen through Day 365
- To compare relative safety among study arms as assessed by systemic and local reactogenicity for 14 days after each vaccination, unsolicited adverse events for 28 days after each vaccination, and serious adverse events (SAE) and medically attended events (MAAE) from Day 1 through Day 57, and related SAE/MAAEs through Day 181.

Exploratory

- To evaluate other measures of the humoral immune responses for each regimen
- To evaluate humoral immune responses of each ID regimen (separately) compared to licensed dose administered SC to monkeypox virus

3.2. Endpoints

Primary

- Vaccinia virus specific Plaque Reduction Neutralization Test (PRNT) GMT at Day 43

Secondary

- Individual peak GMT through Day 365
- Vaccinia virus specific PRNT GMT at Study Day 1, 15, 29, 43, 57, 90, 181, and 365
- Vaccinia virus specific PRNT half-life (t ½)
- Frequency, severity, and relatedness of solicited systemic and local adverse events (AEs) for 14 days after each vaccination.
- Frequency, severity, and relatedness of unsolicited AEs in each study arm for 28 days after each vaccination.
- Frequency and relatedness of Medically Attended Adverse Events (MAAEs) and Serious Adverse Events (SAEs) in each study arm through Day 181.

- Frequency of withdrawals or discontinuation of vaccination in each study arm

Exploratory

- Results from additional immunologic assays for vaccinia and other related viruses.
- Monkeypox virus specific PRNT GMT at Day 1 and 43.

3.3. Study Definitions and Derived Variables

Baseline value will be defined as the last value obtained prior to the first vaccination/dose of study product.

Seroconversion for the Vaccinia virus specific PRNT will be defined as any positive result if negative at baseline or a two-fold increase if positive at baseline.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This study is a Phase 2 randomized, open-label, non-placebo controlled, multi-site clinical trial that will evaluate two ID regimens for MVA-BN vaccine compared to the standard SC regimen in healthy, vaccinia-naïve adults 18 to 50 years of age, inclusive. At least 210 participants will be enrolled and randomized to one of three study arms. The two dose sparing strategies include one-fifth (2×10^7) and one-tenth (1×10^7) of the standard dose of MVA-BN administered ID on Day 1 and 29 (Arm 1 and 2, respectively). The comparator arm (Arm 3) will be the 2-dose standard (1×10^8) MVA-BN SC regimen.

The study will enroll a 1:1:1 randomization allocation. Participants will not be stratified by clinical trial site, demographic characteristics, or Human Immunodeficiency Virus (HIV) infection status; however, these data will be collected during screening and enrollment. Each participant may be screened either in a separate visit in the 7 days prior to Day 1 or on Day 1. Participants will be followed as outlined in the Schedule of Activities. The last follow-up visit will be at about 1 year after the first vaccination. The study design is presented in Table 1.

4.2. Discussion of Study Design, Including the Choice of Control Groups

This study is non-placebo controlled. Dose-sparing regimens will be evaluated in comparison with standard of care.

4.3. Selection of Study Population

This study will enroll healthy, non-pregnant, non-breastfeeding adults 18 to 50 years old. Participants with stable medical conditions and well-controlled HIV infection can participate. The study will aim to enroll a population that has demographic features similar to the population being affected with mpox, yet also reflects the larger U.S. population to ensure broad applicability of the study findings. To this end, the goal will be to enroll:

- at least 30% female participants
- at least 20% African American/Black participants
- at least 20% Hispanic participants

These are enrollment goals and will not be a deviation if these are not met. Sites will be chosen based on projected ability to enroll the representative study population. Enrollment will be monitored and adjusted at individual sites to pursue these goals while also enrolling this study quickly to inform public health decisions.

Participant Inclusion and Exclusion Criteria will be confirmed by an investigator named on the delegation log. If there is any uncertainty, the Principal Investigator (PI) will make the decision on whether a potential participant is eligible for study enrollment. No exemptions will be granted on Inclusion/Exclusion Criteria.

Inclusion Criteria

To be eligible to participate in this study, an individual must meet all the following criteria:

1. Individuals 18 - 50 years of age inclusive at the time of consent.
2. Able to read the written informed consent, states willingness to comply with all study procedures, and is anticipated to be available for all study visits.
3. Agreement to adhere to Lifestyle Considerations during the study.

Note: During this study, participants are asked to:

- *Follow public health guidance on preventing monkeypox infection and notify the clinical site if exposed to an individual with monkeypox.*
- *Contact the clinical site immediately if they develop signs and symptoms consistent with monkeypox to schedule an ad hoc study sick visit.*
- *Refrain from receiving a live vaccine from enrollment through Day 57.*
- *Refrain from receiving any other vaccine through Day 43.*
- *Decline participation in another study evaluating investigational vaccines through Day 181.*
- *Decline participation in another study evaluating an investigational MVA-based vaccine through end of trial.*

Of note, participants may enroll in non-interventional, observational studies (e.g., natural history study of monkeypox). However, concurrent participation in this trial and observational studies can only occur if the recommended blood collection volumes are not exceeded.

4. Females of reproductive potential who have sexual intercourse with males must agree to use highly effective contraception for at least 1 month prior to signing the Informed Consent Form (ICF) and through Day 57.

   Note: See Manual of Procedures (MOP) for definitions and list of highly effective contraception

5. In good general health as evidenced by medical history, physical examination, and clinical judgement of the investigator to be in stable state of health.

   Note: Participants with pre-existing stable chronic medical conditions defined as conditions not requiring significant change in therapy or hospitalization for worsening disease in the 4 weeks prior to enrollment can be included at the discretion of the investigator. This includes stable, well-controlled HIV positive individuals.

6. If HIV infected individual, they must be on suppressive antiretroviral therapy (ART) for at least 6 months, report a CD4 count of greater than 350 cells/μL, and no acquired immunodeficiency syndrome (AIDS)-defining illness in the last year.

Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Ever received a licensed or an investigational smallpox or monkeypox vaccine.

   Note: this includes Dryvax, Acam2000, LC 16 m8, MVA-based vaccine candidate or licensed vaccines, and Jynneos, Imvamune or Imvanex)

2. Any history of monkeypox, cowpox, or vaccinia infection.
3. Close contact of anyone known to have monkeypox in the 3 weeks prior to signing ICF.
4. Immunocompromised as determined by the investigator.
5. Recent or current use of any immunosuppressing medications in the 4 weeks prior to signing ICF.

Note: topical, ophthalmic, inhaled, intranasal, and intraarticular corticosteroids are acceptable, but receipt of ≥20 milligram (mg)/day of prednisone or equivalent for ≥14 consecutive days in the 4 weeks prior to signing ICF is exclusionary.

6. Pregnant or breast feeding.
7. Received or plans to receive a live vaccine in the 4 weeks prior to signing ICF and 4 weeks after each vaccination.
8. Received or plans to receive any other vaccine in the 2 weeks prior to signing ICF through Day 43.
9. Received experimental therapeutic agent or vaccine in the 3 months prior to signing ICF.
10. Has known allergy or history of anaphylaxis or other serious adverse reaction to a vaccine or vaccine products.

    Note: this includes individuals with history of severe allergic reaction to gentamicin, ciprofloxacin, chicken or egg protein.

11. Has tattoos, scars, or other marks which would, in the opinion of the investigator, interfere with assessment of the vaccination site.
12. Has any medical disease or condition that, in the opinion of the participating site PI or appropriate sub-investigator, precludes study participation.

    Note: this includes acute, subacute, intermittent, or chronic medical disease or condition that would place the participant at an unacceptable risk of injury, render the participant unable to meet the requirements of the protocol, or may interfere with the evaluation of responses or the participant's successful completion of this trial.

4.4. Treatments

4.4.1. Treatments Administered

Participants will receive Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, or Subcutaneous MVA-BN 1 x 10^8, administered on Day 1 and Day 29.

4.4.2. Identity of Investigational Product(s)

Product: JYNNEOS is FDA-approved and licensed as a smallpox and mpox vaccine in the United States. The vaccine, when thawed, is a milky, light yellow to pale white colored suspension that is licensed for subcutaneous injection. JYNNEOS is a live vaccine produced from the strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), an attenuated, non-replicating orthopoxvirus. MVA-BN is grown in primary Chicken Embryo Fibroblast (CEF) cells suspended in a serum-free medium containing no material of direct animal origin, harvested from the CEF cells, purified, and concentrated by several Tangential Flow Filtration (TFF) steps including benzonase digestion. Each 0.5 milliliter (mL) dose is formulated to contain 0.5 x 10^8 to 3.95 x 10^8 infectious units of MVA-BN live virus in 10 millimolar (mM) Tris (tromethamine), 140 mM sodium chloride at pH 7.7. Each 0.5 mL dose may contain residual amounts of host-cell DNA (≤ 20 microgram (mcg)), protein (≤ 500 mcg), benzonase (≤0.0025 mcg), gentamicin (≤0.163 mcg), and ciprofloxacin (≤0.005 mcg).

4.4.3. Method of Assigning Participants to Treatment Groups (Randomization)

Enrollment/randomization will be performed through the enrollment module in the electronic data capture system, maintained by the Statistical and Data Coordinating Center (SDCC). Eligible participants will be randomized and assigned in a 1:1:1 ratio to Intradermal MVA-BN 2 x 10^7: Intradermal MVA-BN 1 x 10^7: Subcutaneous MVA-BN 1 x 10^8, with no stratification by site or other factors. The randomization is based on a variable blocked scheme to provide an approximately balanced allocation to the treatment groups during the study.

4.4.4. Selection of Doses in the Study

This study uses the FDA-approved, licensed dose 1 x 10^8 administered SC on Day 1 and 29 as the comparator for the ID doses of MVA-BN. The ID regimens being evaluated in this study use lower doses of the licensed vaccine, and either match or are one dilution lower than the dose used in the prior ID dosing study (PubMed reference number (PMID) 26143613). Therefore, it is anticipated this range is safe and immunogenic.

4.4.5. Selection and Timing of Dose for Each Participant

All participants will receive two doses of MVA-BN on Day 1 and Day 29. This is the FDA-approved, licensed dosing schedule for MVA-BN.

4.4.6. Blinding

This study will not utilize blinding or masking procedures as it is an open-label, non-placebo-controlled trial. Research laboratories will be blinded to participant study arm for the purposes of immunogenicity evaluations.

4.4.7. Prior and Concomitant Therapy

At screening (i.e., the screening visit or Day 1 visit if the screening visit is not conducted), participants will be asked about receipt of immunosuppressive therapy, experimental therapeutic agents and vaccines, other medications, and vaccines. At each subsequent study visit through Day 57, new concomitant medication(s) and changes to existing medications will be recorded as well as receipt of a non-study vaccine. For this study, concomitant medications to be reported in the Case Report Form (CRF) are prescription drugs, over-the-counter medications, and supplements. Concomitant medications taken and vaccines received in the 4 weeks prior to providing informed consent will be recorded in the CRF. Any drug taken or non-study vaccine received by the participant during the trial should be recorded on the appropriate CRF through Day 57. Concomitant medications that are associated with a SAE or MAAE deemed related to study product and clinically relevant to report will be recorded in the CRF through Day 181. An exception to this schedule for recording concomitant therapy is during sick visits for those who have laboratory-confirmed mpox (illness). During sick visits, concomitant medications and treatments will be collected. Sick visits will be reported in Listing 12.

Medications that might interfere with the evaluation of the immune response to MVA-BN should not be used by the participant during the study-reporting period unless clinically indicated as part of the participant's health care for a condition diagnosed after enrollment. This would include any systemic immunosuppressant medication that may impact the immunogenicity endpoints. In the event medical conditions dictate the use of these medications, participants are encouraged to obtain adequate care, comply with the course of therapy as prescribed by their physician and inform the study Investigator as soon as practical.

4.4.8. Treatment Compliance

All participants will receive two doses of study product administered in the clinic. Participants will be directly observed at the time of dosing by a member of the clinical research team who is licensed to administer vaccines. Improper administration such as indicated by lack of formation of a wheal at the injection site will be reported as a protocol deviation.

4.5. Immunogenicity and Safety Variables

See Table 2 for a schedule of study procedures.

Multiple observations within a specific visit period are accepted. In the case of multiple observations within a specific window, the assessment value that is closest to the scheduled visit window will be used in the analyses for the post-baseline records. For screening and baseline visits, the last assessment value prior to the administration of study product will be used. All the recorded data will be listed. If observations have the same distance to the scheduled assessment, the latest one will be used.

4.5.1. Safety Variables

Adverse Events (AE): Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not it is considered intervention-related (21 Code of Federal Regulations (CFR) 312.32 (a)). An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of medicinal(investigational) product.

Any medical condition that is present at the time the participant is screened will be considered as baseline and not reported as an AE. However, if the severity (i.e., grade) of any pre-existing medical condition increases, it will be recorded as an AE.

Adverse events can be further divided into solicited adverse events and unsolicited adverse events. Solicited adverse events are those for which the study team will specifically query the participant whether they occurred. Unsolicited adverse events are those events that the participant report occurring without being queried about the specific event.

AEs will be followed through resolution.

Solicited Adverse Events: Reactogenicity will be especially important to document because of prior studies demonstrating more local reactogenicity among participants who received the ID MVA-BN vaccine injection. In this study, we will collect the following solicited adverse events based on prior studies. This includes local (pain at the site of the injection, erythema/redness, induration/swelling, pruritis) and systemic (fever, chills, nausea, headache, fatigue, change in appetite, myalgia [exclusive of the injection site], and arthralgia) reactogenicity. In addition, we expect that some participants will develop skin discoloration and nodules which will be reported as AEs and not collected on the memory aid and followed through to resolution. For this study, we will use the following toxicity grading scale: "*FDA Guidance for Industry, Toxicity Grading Scale for Healthy Adults and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials*" as a reference. Of note, pruritis/itching, arthralgia, chills, and change in appetite are not included in the FDA toxicity table and will be graded according to Table 5. Additional clarification of induration grading is provided in Table 6.

Systemic and local solicited adverse events will be collected from Day 1 through Day 15, and Day 29 through Day 43. However, participants with ongoing systemic and/or local reactogenicity at Day 15 or Day 43 visit,

will be asked to measure erythema/redness and/or induration/swelling until it has resolved, if applicable, and record end date of all other signs and symptoms.

Unsolicited Adverse Events: Unsolicited events are all AEs spontaneously reported by the participant and/or in response to an open question from study personnel or revealed by observation, physical examination or other diagnostic procedures.

Unsolicited adverse events will be collected from Day 1 through Day 29, and Day 29 through Day 57.

Serious Adverse Events (SAE): An adverse event or suspected adverse reaction will be considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes (21 CFR 312.32 (a)):

- death
- a life-threatening adverse event*
- inpatient hospitalization or prolongation of existing hospitalization
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or
- a congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, convulsions that do not result in inpatient hospitalization, etc.

* An adverse event is considered “life-threatening” if, in the view of either the investigator or sponsor, its occurrence places the patient or participant at immediate risk of death. It does not include grade 4 severity unless the adverse event might have caused death.

All SAEs will be collected from Day 1 through Day 57 and all SAEs related to the vaccine will be collected through Day 181. All SAEs will be followed through resolution or until the site investigator deems the event to be chronic or deems the participant is stable.

Medically Attended Adverse Events (MAAE): A medically attended adverse event (MAAE) is an unsolicited AE that results in unscheduled medical attention such as a hospitalization for less than 24 hours, an emergency room visit, or an otherwise unscheduled healthcare visit for any reason. All MAAEs will be collected from Day 1 through Day 57, and all MAAEs related to the vaccine through Day 181.

Suspected Unexpected Serious Adverse Reactions (SUSAR): A SUSAR is a SAE that is considered related to the study product and is unexpected. Unexpectedness to study product will be determined by what is listed in the JYNNEOS package insert. SUSAR will be collected during the same time period as other SAEs and followed as above.

Severity: All AEs including SAEs will be assessed for severity according to the toxicity grading scale; FDA Guidance for Industry, Toxicity Grading Scale for Healthy Adults and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials. For adverse events (AEs) not included in the protocol-defined grading scale, the following guidelines will be used to describe severity:

Mild (Grade 1): Events that are usually transient and may require only minimal or no treatment or therapeutic intervention and generally do not interfere with the participant’s usual activities of daily living.

Moderate (Grade 2): Events that are usually alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the research participant.

Severe (Grade 3): Events interrupt usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention. Severe events are usually incapacitating.

Life-threatening (Grade 4): Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required, hospitalization or care provided.

Relationship to Study Intervention: For each reported adverse event or reaction, the Principal Investigator or designee will assess the relationship of the event to the study product using the following guideline:

Related: The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event.

Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.

Not Related: There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

Pregnancies: Pregnancy is not an AE. However, any pregnancies reported during study participation (through Day 365) will be followed for safety and outcome. This follow-up will include pregnancy outcome (termination, pre-term birth, term birth) and newborn outcome (live birth, fetal demise, stillbirth, presence of any congenital anomalies). No in-person visits will be required for pregnancy outcome determination.

Unanticipated Problems: The Department of Health and Human Services Office for Human Research Protections (OHRP) considers unanticipated problems (UPs) involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied; and
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Incidents arising from noncompliance with study procedures will be reported as protocol deviations. An incident that qualifies as both a UP and a protocol deviation will be reported as both.

4.5.2. Immunogenicity Variables

The Bavarian Nordic (BN) Vaccinia virus Western Reserve strain (VV-WR) plaque reduction neutralizing antibody (PRNT) assay will be used as the primary assay to determine immunogenicity. A minimum of 4 timepoints (Days 1, 29, 43, 90) will be tested by Bavarian Nordic in duplicate and the results average. The limit of detection (LOD) and lower limit of quantification (LLOQ) for this assay is 20 titer units and the upper limit of quantification (ULOQ) is not applicable. Results below the LOD/LLOQ will be imputed as one-half

the LOD/LLOQ. Additional timepoints (Days 15, 57, 181 and/or 365) will be evaluated as able (given lab throughput and cost).

This study will also measure a mpox virus specific PRNT and will test a minimum of 2 timepoints (Days 1 and 43). Additional timepoints (Days 15, 29, 57, 90, 181 and/or 365) will be evaluated as able (given lab throughput and cost). The mpox PRNT assay is currently in development at Battelle. LOD, LLOQ, and ULOQ values have yet to be established. They will be reported in the CSR. Results below the LOD will be imputed as one-half the LOD.

Additional exploratory assessments of humoral immunity including Enzyme-linked Immunosorbent Assays (ELISAs) may be performed on samples from this trial.

5. SAMPLE SIZE CONSIDERATIONS

Approximately 210 participants in the modified intention to treat population (mITT) (70 per study arm; 140 total for each test of non-inferiority) will provide ample power for both tests of non-inferiority with a type I error rate of 0.05 (Table 3), and assumes, conservatively, that both arms have a standard deviation of 0.6.

A sample size of 140 total for the test of non-inferiority will provide 84% power with the noninferiority (NI) margin of 0.5 and two-sided type I error rate of 0.05. Power calculations conservatively assume a standard deviation of 0.6 in both arms. Data from prior studies by Pittman [14] and Frey [12] suggest that the standard deviation will be lower than 0.6 at later expected peak times, in which case power should be higher for the non-inferiority tests. Note that the power is expected to be lower for the comparison of the 1 x 10^7 ID regimen and the standard dose regimen for two reasons: 1) the hypothesis test is conditional on rejecting the null hypothesis comparing the 2 x 10^7 ID arm to the standard regimen arm, and 2) the true GMT for the 1 x 10^7 ID may be less than the standard SC dose.

In a prior study that compared ID and SC routes of MVA-BN [13], 10% of the randomized participants did not receive the second vaccination. Therefore, this trial will enroll up to 231 participants (210 x 1.1) with the goal of having 210 participants retained through Day 43 to evaluate the primary endpoint.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum, and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for categorical measures. In general, all data will be listed, sorted by treatment, and participant, and when appropriate by visit number within participant. Summary tables will be structured with a column for each treatment in the order Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, Subcutaneous MVA-BN 1 x 10^8, and will be annotated with the total population size relevant to that table/treatment.

6.2. Timing of Analyses

The interim analysis will be performed after all participants have been followed through Study Day 181. The following tables and figures will be included in the interim analysis: Table 7, Table 8, Table 13, Table 14, Table 16, Table 18, and Figure 11 (Day 1, Day 15, Day 29, Day 43, Day 57, Day 90, Day 181 timepoints only), Table 22 and Figure 13 (Day 1 and Day 43 timepoints only), Table 28, Table 30, Table 40, Table 42, Figure 15, and Figure 17 (Day 1, Day 43, and Day 90 timepoints only), Table 48 and Figure 19 (Day 43 timepoint only), and Table 51, Table 53, Table 54, Table 55, Table 56, Table 57, Table 75, Table 76, Table 77, and Table 81.

The final analysis will be performed after database lock.

6.3. Analysis Populations

Summaries and analysis of safety data will be presented for the Safety Population. Summaries and analysis of immunogenicity data will be presented for the mITT Population and, if there are protocol deviations which may affect analysis, the Per Protocol Population. The composition of analysis populations, including reasons for participant exclusion, by treatment arm, is presented in Table 8. A listing of all participants, visits, and observations excluded from the analysis populations will be provided in the CSR (Listing 5).

6.3.1. Modified Intention-to-Treat (mITT) Population

The modified intent-to-treat (mITT) population includes all participants who received at least one dose of vaccine and contributed both pre- and at least one post-vaccination venous blood sample for immunogenicity testing for which valid results were reported.

In the event any participants do not receive the treatment to which they were randomized, they will be analyzed according to the study product received.

6.3.2. Per Protocol Population

The per protocol (PP) population will be defined as all participants in the mITT subset with the following exclusions:

- Data from all available visits for participants found to be ineligible at baseline.
- Data from all visits after the protocol deviations that are considered to affect the science (as determined by the sponsor at an ad hoc meeting).
- Data from any visit that occurs substantially out of window. Substantially out of window will be defined as a visit occurring three or more days outside of the visit window. Visit windows for

visits post dose 2 will be adjusted to reflect the actual date of receipt of Dose 2 not based on days post dose 1.

In the event any participants do not receive the treatment to which they were randomized, they will be analyzed according to the study product received.

6.3.3. Safety Population

The safety analysis population will include all enrolled participants who receive at least one dose of study vaccine. In the event any participants do not receive the treatment to which they were randomized, they will be analyzed according to the study product received.

6.4. Covariates and Subgroups

The protocol does not define any formal subgroup analyses, and the study is not adequately powered to perform subgroup analyses.

6.5. Missing Data

All attempts will be made to collect all data per protocol. No imputation will be performed for missing values. Any data point that appears to be erroneous or inexplicable based on clinical judgment will be investigated as a possible outlier. If data points are identified as outliers, sensitivity analyses will be performed to examine the impact of including or excluding the outliers. Any substantive differences in these analyses will be reported.

6.6. Interim Analyses and Data Monitoring

6.6.1. Safety Review

Safety oversight will be conducted by a Data Safety Monitoring Board (DSMB) that is an independent group of experts that monitors participant safety and advises the Division of Microbiology and Infectious Diseases (DMID). The DSMB members will be separate and independent of study personnel conducting this trial and have appropriate expertise to contribute to the interpretation of the data from this trial. The DSMB will operate under the rules of a DMID-approved charter written at the organizational meeting of the DSMB. Reports may include enrollment and demographic information and solicited and unsolicited AE/SAEs. The DSMB will review SAEs on a regular basis and ad hoc during this trial. The DMID Medical Monitor will be responsible for reviewing SAEs in real time. The DSMB will conduct the following reviews:

- Approximately Day 22-29 after study start. Given the planned short enrollment period (3-4 weeks) and second dose of vaccine given on day 29, there is a narrow window for review. As such the review will focus on AEs utilizing real time reports where able.
- Ad hoc meeting:
  - When trial-level halting criteria are met.
  - At the request of DMID to review a potential safety concern identified in the trial.
- Interim and final data will be shared with the DSMB, but the DSMB does not need to meet to review the final data.

Additional data may be requested by the DSMB. As an outcome of each review/meeting, the DSMB will make a recommendation as to the advisability of proceeding with study interventions (as applicable), and to

continue, modify, or terminate this trial. The DSMB will review applicable data to include, but not limited to, study progress and participant, clinical, safety and safety related data. DMID or the DSMB chair may convene the DSMB on an ad hoc basis according to protocol criteria or if there are immediate concerns regarding observations during the course of this trial.

The DMID Medical Monitor is empowered to stop enrollment and study product administration if AEs that meet the halting criteria are reported.

Study Halting Criteria

The study will be paused for safety analysis if any of the following events occur:

- One (1) participant experiences a SAE after the administration of the vaccine that is considered related to the vaccine.
- One (1) participant experiences a Grade 4 solicited AE after the administration of the vaccine that is considered related to the vaccine.
- Three (3) or more participants experience a Grade 3 or higher unsolicited AE coded to the same Preferred Term based on the Medical Dictionary for Regulatory Activities (MedDRA) that are deemed related to the vaccine.

Individual Halting Criteria

If a single participant meets an individual halting criterion, this will not halt the whole study but halts the participant's involvement in terms of the administration of the second dose of the vaccine. However, while the participant is discontinued from receipt of vaccine, they should be encouraged to remain in the study to monitor safety and evaluate immunogenicity until the end of the study.

1. Any participant experiences laryngospasm, bronchospasm or anaphylaxis within 24 hours after the administration of the vaccine that is considered related to the vaccine within the 24 hours after vaccination.
2. Any participant experiences generalized urticaria (defined as urticarial lesions occurring at more than two body parts) within 3 days after the administration of the vaccine.
3. Any participant experiences any Grade 4 solicited AE or an SAE after the administration of the vaccine that is deemed related to the vaccine.
4. Any participant that experiences ulceration, abscess or necrosis at the injection site that is considered related to the vaccine administration.

A participant may be removed from the study if the investigator or the medical monitor deems it in the best interest of the participant. The participant could be withdrawn from the study at any time during the trial.

6.6.2. Immunogenicity Interim Analysis

After all participants have completed Day 181, analysis of the primary outcome will proceed. The risk of introducing bias prior to data freeze is considered small and outweighed by the benefits of informing public health decisions during this global public health crisis. The study team may disseminate this data to public health officials and partners as needed and include it in publications and presentations to inform the global scientific community prior to the conclusion of the study.

6.7. Multicenter Studies

Data will be pooled across all clinical sites. Center effects are not anticipated because the sites are using standardized procedures for vaccination and assessment of solicited and unsolicited adverse events, and the study relies on central laboratories for the assessment of immunogenicity endpoints.

6.8. Multiple Comparisons/Multiplicity

No adjustments for multiple testing are planned.

7. STUDY PARTICIPANTS

7.1. Disposition of Participants

Table 10 will present a summary of the reasons that participants were screened but not enrolled. The composition of analysis populations, including reasons for participant exclusion, by treatment arm, is presented in Table 8.

The disposition of participants in the study will be tabulated and treatment group (Table 7). The table shows the total number of participants screened, enrolled/randomized, receiving at least 1 dose, receiving 2 doses, completing the primary endpoint (Day 43), completing the final blood draw (Day 365), completing follow-up (Day 365), and completing follow-up per protocol.

A flowchart showing the disposition of study participants, adapted from the Consort Statement [15] will be included (Figure 1). This figure will present the number of participants screened, enrolled, lost to follow-up, and analyzed, by treatment arm.

A listing of participants who discontinued dosing or terminated from study follow-up and the reason will be included in Listing 2.

7.2. Protocol Deviations

A summary of participant-specific protocol deviations will be presented by the reason for the deviation, the deviation category, and treatment group for all participants (Table 4). Deviations will be reviewed for possible participant exclusion from the per protocol population. All participant-specific protocol deviations and non-participant specific protocol deviations will be included in Appendix 3 as data listings (Listing 3 and Listing 4, respectively).

8. IMMUNOGENICITY EVALUATION

All immunogenicity variables will be listed by treatment group, participant, and visit (Listing 8). N, geometric Mean, and 95% CI will summarize continuous immunogenicity variables. Immunogenicity data summaries and analysis will be presented for the mITT population and, if there are protocol deviations which may affect the analysis, the PP population.

Immune response will be presented graphically using reverse cumulative distribution (RCD) curves (Figure 3, Figure 4, Figure 5, Figure 6, Figure 7, Figure 8, Figure 9, and Figure 10), and longitudinal presentation of GMTs (Figure 11, Figure 12, Figure 13, Figure 14, Figure 15, Figure 16, Figure 17, and Figure 18).

8.1. Primary Immunogenicity Analysis

Vaccinia virus specific PRNT

GMTs and corresponding 95% confidence intervals (CIs) will be reported by study arm at Days 1 and 43 in Table 24 (mITT population) and Table 25 (PP population).

GMT Ratio, defined as the ratio of each ID arm to the control SC arm, and corresponding 95% CIs (using Student's t distribution) will be reported at Day 1 and 43 in Table 32 (mITT population) and Table 33 (PP population).

Geometric Mean Fold Rises (GMFRs) from baseline with corresponding 95% CIs and percent of participants with seroconversion with corresponding 95% CIs will be reported by study arm at Day 43 in Table 36 (mITT population) and Table 37 (PP population).

Days 15, 29, 57, 90, 181 and/or 365 may also be reported in all the above tables if possible given lab throughput and cost.

Primary Hypothesis

The primary hypothesis involves a two-step hierarchical process. The study will first test noninferiority of the 2 x 10^7 $TCID_{50}$ ID regimen relative the standard dose regimen, to 1 x 10^8 $TCID_{50}$ SC. If the 2 x 10^7 ID regimen is non-inferior to the standard dose regimen, hypothesis testing will proceed to test non-inferiority of the 1 x 10^7 $TCID_{50}$ ID regimen relative to the standard dose regimen. The results of these tests will be presented in Table 16 and Table 17.

Hypothesis testing will be stepwise, starting with the non-inferiority test of the 2 x 10^7 $TCID_{50}$ ID regimen relative to standard regimen, with an unequal-variance, two-sample t-test statistic and 95% two-sided confidence intervals. The ID-dose regimen will be considered non-inferior if the 95% confidence interval of the geometric mean titer ratio (obtained by calculating the antilog of the difference in the mean log10-transformed titers) is entirely above 0.5. The selection of this NI margin was based on the pivotal Phase 3 trial by Pittman et al., in 2019 comparing one dose of ACAM2000 and the now licensed 2-dose standard MVA-BN regimen, which provided an estimated relative (peak) immune response of approximately 2-times higher for MVA-BN [14]. An NI margin of 0.5 will correspond an immune response of the lower-dose MVA-BN at least as high as what would be expected for ACAM2000.

If the null hypothesis from analysis 1 is rejected in favor of non-inferiority (i.e., the lower limit of the 95% CI of the difference in log of GMTs for 2 x 10^7 $TCID_{50}$ MVA-BN ID compared to 1 x 10^8 $TCID_{50}$ MVA-BN SC is greater than log(0.5) which is equal to -0.301), testing will proceed with a noninferiority test of the 1 x 10^7 $TCID_{50}$ MVA-BN ID regimen relative to the standard dose regimen, using an unequal variance, two-sample t-test statistic with 95% confidence interval.

8.2. Secondary Immunogenicity Analyses

Secondary Hypotheses

- At Day 365 the humoral immune response of the 2 x 10^7 MVA-BN ID regimen will be non-inferior to the standard 1 x 10^8 MVA-BN SC regimen, as assessed by PRNT GMT.
- At Day 365 the humoral immune response of the 1 x 10^7 MVA-BN ID regimen will be non-inferior to the standard 1 x 10^8 MVA-BN SC regimen, as assessed by PRNT GMT.
- The humoral immune responses, as assessed by PRNT GMT, for each ID regimen will be similar to the SC regimen at all study days. [Note, this corresponds to two hypotheses, one for each ID study arm.]
- The humoral immune responses, as assessed by vaccinia specific PRNT half-life, for each ID regimen will be similar to the SC regimen. [Note, this corresponds to two hypotheses, one for each ID study arm.]
- The humoral immune responses, as assessed by monkeypox specific PRNT GMT, for each ID regimen will be similar to the SC regimen at Day 1 and 43. [Note, this corresponds to two hypotheses, one for each ID study arm.]

The results of these tests will be presented in Table 18, Table 20, and Table 22 (mITT population); and Table 19, Table 21, and Table 23 (PP population).

8.3. Exploratory Immunogenicity Analyses

Monkeypox virus specific PRNT

GMTs and corresponding 95% CIs will be reported by study arm at Days 1 and 43 in Table 26 (mITT population and Table 27 (PP population).

GMT Ratio, defined as the ratio of each ID arm to the control SC arm, and corresponding 95% CIs will be reported at Day 1 and 43 in Table 34 (mITT population) and Table 35 (PP population).

GMFRs from baseline and corresponding 95% CIs will be reported by study arm at Day 43 in Table 38 (mITT population) and Table 39 (PP population).

Days 15, 29, 57, 90, 181 and/or 365 may also be reported in all the above tables if possible given lab throughput and cost.

The ratio of Monkeypox virus specific PRNT to Vaccinia virus specific PRNT will also be presented in Table 44 (GMT, mITT population), Table 45 (GMT, PP population), Table 46 (GMFR, mITT population), and Table 47 (GMFR, PP population).

Other Assays

Additional assessments of humoral immunity including ELISAs, if performed, will be presented in the same formats starting with Table 24 and ending with Table 35, and Figure 3, Figure 4, Figure 5, Figure 6, Figure 7, Figure 8, Figure 9, Figure 10; and included in Listing 8.

Assay development data for Anti-MVA Neutralizing Antibody and Anti-MPXV clade I Neutralizing Antibody assays will be included in the interim analysis (Table 28, Table 29, Table 30, Table 31, Table 40, Table 41, Table 42, Table 43, Figure 15, Figure 16, Figure 17, and Figure 18).

Comparison of Immunogenicity Responses

Spearman rank correlations with 95% CI for immunogenicity responses at Day 43 will be presented by treatment group (Table 48, Table 49, Figure 19, and Figure 20).

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex at birth, gender identity, sexual identity, ethnicity, race, and HIV-status will be presented by treatment group overall and by site (Table 11, Table 12, Table 13, and Table 14). Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with the National Institutes of Health (NIH) reporting policy, participants may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option.

Individual participant listings (Appendix 3) will be presented for all demographics (Listing 6); pre-existing medical conditions (Listing 7); vital signs and oral temperature (Listing 13); and concomitant medications (Listing 15).

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and past pre-existing medical conditions will be MedDRA® coded using MedDRA dictionary version 24.0 or higher. Summaries of participants' pre-existing medical conditions will be presented by treatment group (Table 15). Individual participant listings will be presented for all medical conditions (Listing 7).

9.1.2. Prior and Concomitant Medications

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by World Health Organization (WHO) Drug Terms 2 and 3 and treatment group (Table 87).

Individual participant listings will be presented for all concomitant medications (Listing 15).

9.2. Measurements of Treatment Compliance

The number of doses of study product administered to participants will be presented by treatment group as part of the participant disposition table (Table 7). Table 9 presents the number of participants who received their first dose, by site and treatment arm. Timing of first dose by treatment arm will also be presented graphically (Figure 2).

9.3. Adverse Events

When calculating the incidence of adverse events (i.e., on a per participant basis), each participant will only be counted once and any repetitions of adverse events within a participant will be ignored; the denominator will be the total population size. All adverse events reported will be included in the summaries and analyses.

A summary comparing safety events contributing to the secondary safety outcomes by treatment arm is presented in Table 50. A summary of all safety events is presented in Table 51.

9.3.1. Solicited Events and Symptoms

Systemic solicited adverse events will be collected pre-vaccination, and systemic and local solicited adverse events were collected 30 minutes post-vaccination and then daily for 15 days after each vaccination. Solicited adverse events will be graded on a scale of 0 (none), 1 (mild), 2 (moderate), 3 (severe), and 4 (life-threatening). Systemic events include fever, chills, nausea, headache, fatigue, change in appetite, myalgia (exclusive of the injection site), and arthralgia. Local events include pain at injection site, erythema/redness, induration/swelling, and pruritis at injection site.

The proportion of participants reporting at least one solicited adverse event will be summarized for each solicited adverse event, any systemic symptom, any local symptom, and any symptoms (Table 53). The 95% CI calculated using Clopper-Pearson methodology from a binomial distribution (SAS Proc Freq with a binomial option) will be presented (Table 54).

For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 14 days after each vaccination will be summarized for the Safety Population. The number and percentage of participants reporting each event will be summarized by the maximum severity and treatment group, separately for each vaccination and over all vaccinations. For each event the denominator is the number of participants with non-missing data for the specific event (Table 55, Table 56, and Table 57).

The number of participants reporting a solicited adverse event will be summarized for each day post vaccination for each vaccination and for all vaccinations combined both in summary tables (starting with Table 58 and ending with Table 69) and graphically in a bar chart (Figure 21, Figure 22, Figure 23, Figure 24, Figure 25, and Figure 26). A comparison of the event rate for each treatment group between vaccination 1 and vaccination 2 will be presented (Table 70).

Solicited adverse events by participant will be presented in Listing 9 and Listing 10.

Duration of erythema/redness will be presented by vaccination and treatment group in Table 81.

9.3.2. Unsolicited Adverse Events

The proportion of participants reporting at least one unsolicited adverse event will be summarized by MedDRA system organ class and preferred term for each vaccination and over all vaccinations. Denominators for percentages are the number of participants who received the vaccination being summarized.

Adverse events by participant will be presented in Listing 11.

The following summaries for unsolicited adverse events will be presented by MedDRA system organ class, preferred term, vaccination, and treatment group:

- Summary of adverse events occurring in 5% of participants (Table 52)
- Participant incidence and total frequency of adverse events over time by dose with 95% CI (Days 1-15, Days > 15) (Table 71 , Table 72 , and Table 73)
- Summary of severity and relationship to study product (Table 74)
- Participant incidence and total frequency of related adverse events over time (Days 1-15, Days > 15) (Table 75 , Table 76 , and Table 77)
- Participant listing of non-serious adverse events of moderate or greater severity (Table 79)
- Listing of other significant adverse events, Medically Attended Adverse Events (MAAEs) and Unanticipated Problems (UPs) (Table 80)
- Bar chart of non-serious related adverse events by severity and MedDRA system organ class (Figure 27)
- Bar chart of non-serious related adverse events by severity (Figure 28)

Duration of injection site AEs will be presented by vaccination and treatment group in Table 81 .

9.4. Deaths, Serious Adverse Events and other Significant Adverse Events

The following listing will include Participant ID, Age (years), Adverse Event Description, Adverse Event Onset Date/End Date, Last Dose Received/Days Post Dose, Reason Reported as an SAE, Relationship to Treatment, Alternate Etiology if not Related, Outcome, and Duration of Event (days):

- Deaths and Serious Adverse Events (including SUSARs) (Table 78)

9.5. Pregnancies

For any participants in the Safety population who become pregnant during the study, every attempt will be made to follow these participants to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. A table summarizing the total number of pregnancies, number of live births, and number of spontaneous abortions, elective abortions, or still births by treatment will be presented. In addition, a listing of pregnancies and outcomes will be presented (Listing 16, Listing 17, Listing 18, Listing 19, and Listing 20).

9.6. Clinical Laboratory Evaluations

Not applicable.

9.7. Vital Signs and Physical Evaluations

Vital sign measurements include systolic blood pressure, diastolic blood pressure, pulse, and oral temperature. Vital signs will be assessed at Day 1 and Day 29 prior to vaccination and as needed at other study visits if interim change in medical status reported by participant. Vital signs will be tabulated by visit and treatment group (Table 82, Table 83, Table 84, Table 85, and Table 86).

Physical Examinations will be performed at Day 1, Day 15, Day 29, Day 43, and as needed at other study visits if interim change in medical status reported by participant. The following body system will be assessed: Skin. Other body systems may be assessed if indicated (Listing 14Listing 14).

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification (ATC) using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-participant listing of concomitant medication use will be presented (Listing 15). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and treatment group for the Safety population (Table 87).

9.9. Other Safety Measures

Participant Tolerability Assessment: Participants will be asked several yes/no global assessment questions to evaluate how well the vaccine is tolerated and asked to provide a reason for "No" answers.

At Day 15:

- "Based on your experience with the first dose of the vaccine, do you plan to receive your second dose of vaccine in the study on day 29? If No, why?"

At Day 43:

- "Based on your experience with the study vaccine, would you be willing to take it again if recommended by your healthcare provider? If No, why?"
- "Based on your experience with the study vaccine, would you recommend it to a family member or friend if it was recommended by their healthcare provider? If No, why?"

The numbers and percentages of participants willing to receive a second dose, willing to take the vaccine again after receiving both doses, and willing to recommend the vaccine to family/friends after receiving both doses will be reported by treatment group in Table 88. The Sponsor will adjudicate categorization of participant reasons for "No" response and the most common categories of reasons will also be summarized by treatment group in Table 88. Reasons will be listed verbatim in Listing 21.

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

See Section 8.

12. OTHER ANALYSES

Not applicable.

13. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001." The mean, standard deviation, and other statistics will be reported to 1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data. Proportions will be presented as 2 decimal places; values greater than zero but <0.01 will be presented as "<0.01." Percentages will be reported to the nearest whole number; values greater than zero but < 1% will be presented as "<1%;" values greater than 99% but less than 100% will be reported as >99%. PRNT half-life will be calculated as in Frey et al [12].

14. TECHNICAL DETAILS

SAS version 9.4 or above will be used to generate all tables, figures, and listings.

15. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

The protocol stated that the interim analysis would be conducted post-Day 43. The interim analysis was delayed until post-Day 181. A protocol amendment including this change was submitted.

Seroconversion for the Vaccinia virus specific PRNT and ratio of Monkeypox virus specific PRNT to Vaccinia virus specific PRNT will be analyzed. This was not prespecified in the protocol for Stage 1, but was described for Stage 2 when the protocol was amended.

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17. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendix 1, Appendix 2, and Appendix 3.

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

9.1 Overall Study Design and Plan Description

Table 1: Study Design

Study Arm	Dose of JYNNEOS (MVA-BN)	Route of Administration*	Vaccination Day	
			Day 1	Day 29
1	2 x 10^7 $TCID_{50,}$ (0.1 mL)	Intradermal	X	X
2	1 x 10^7 $TCID_{50,}$ (0.05 mL)	Intradermal	X	X
3	1 x 10^8 $TCID_{50,}$ (0.5 mL)	Subcutaneous	X	X
*Subcutaneous is administered in the deltoid region, intradermal is administered in the volar aspect (inner side) of the forearm.				

9.5.1 Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures

Procedures	Optional Screening Visit Day -7 to -1	Enrollment / Baseline Visit 1 Day 1	Visit 2 Day 15 +/- 3 day	Visit 3 Day 29 +/- 3 days	Visit 4 Day 43 +/- 3 days	Visit 5 Day 57 +/- 3 days	Visit 6 Day 90 +/- 5 days	Visit 7 Day 181 +/- 7 days	Visit 8 Day 365 +/- 14 days	Sick/ Unscheduled Visit [6]
Informed consent	X	X[1]								
Demographics	X	X[1]								
Medical history	X	X[1]	X	X	X	X	X	X	X	X
Randomization		X								
Vaccine administration		X		X						
Targeted physical exam	X	X[1]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]
Vital signs	X	X[1]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]
Concomitant medication review	X	X[1]	X	X	X	X	X[3]	X[3]		X[3]
SAE/ MAAEs [4]		All SAE/MAAEs, Days 1 through 57					Only related SAE/MAAEs Days 58 -181			X[4]
Unsolicited AEs[4]		Day 1 through Day 29 and Day 29 through Day 57								X[4]
Solicited (Local and Systemic) AEs		Day 1 through Day 15		Day 29 through Day 43						X[4]
Tolerability Assessment			X		X					
Pregnancy test [5]	X	X[1]		X						
Blood volume per visit (ml)		32	20	20	32	20	20	20	20	20
Blood volume total (ml)		32	52	72	104	124	144	164	184	204

[1] If there is no screening visit, these activities should be conducted at the Day 1 visit prior to randomization. Temperature should be collected on Day 1 and 29 pre-vaccination for all participants.
[2] A targeted (symptom-driven) physical exam will be done at screening (i.e., screening visit or Day 1), on Days 15, 29, and 43 (at least assessment of vaccination site and presence of skin discoloration and nodules will be done), and as needed in all other visits if interim change in medical status reported by participant. Vital signs will be done at screening and on Day 1 and 29 prior to vaccination and on an as needed basis during all other visits.
[3] After Day 57, only concomitant medications that are associated with a related SAE or MAAE (detected through Day 181) and clinically relevant to report, will be recorded in the CRF. An exception to this rule for recording concomitant medications is for sick visits. During sick visits, concomitant medications will be collected.

[4] If SAE/MAAE or unsolicited AE are reported during a sick visit and within the reporting window, it will be reported as AE. See more information about collection of AEs in the safety section of the protocol.
[5] A pregnancy test will be done at the screening visit (if conducted) and on Day 1 prior to randomization. If there is no screening visit, then pregnancy test done will be done on Day 1 only. Participants of childbearing potential must have negative serum or urine pregnancy test in the 24 hours prior to Day 1 and 29 study vaccinations and results confirmed prior to randomization.
[6] Participants reporting monkeypox-like illness and who have a laboratory-confirmed monkeypox will be seen at an ad hoc sick visit. An unscheduled visit may also occur for reasons including, but not limited to, AE follow up, blood draw, or early termination final visit.

9.7.1 Sample Size

Table 3: Sample Size/Probability Estimates

NI margin	Sample Size per arm	Total sample size for NI test	Power
0.5 $Log_{10}(0.5) = -0.301$	60	120	0.78
0.5	70	140	0.84
0.5	80	160	0.88
0.5	85	170	0.90
0.5	90	180	0.92

10.2 Protocol Deviations

Table 4: Distribution of Protocol Deviations by Category, Type, and Treatment Group

Category	Deviation Type	Intradermal MVA-BN 2×10^7 (N=X)		Intradermal MVA-BN 1×10^7 (N=X)		Subcutaneous MVA-BN 1×10^8 (N=X)		All Participants (N=X)	
		Number of Participants	Number of Deviations	Number of Participants	Number of Deviations	Number of Participants	Number of Deviations	Number of Participants	Number of Deviations
Eligibility/ enrollment	Any type								
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x
	Met exclusion criterion								
	ICF not signed prior to study procedures								
	Other								
Treatment administration schedule	Any type								
	Out of window visit								
	Missed visit/visit not conducted								
	Missed treatment administration								
	Delayed treatment administration								
	Other								
Follow-up visit schedule	Any type								
	Out of window visit								
	Missed visit/visit not conducted								
	Other								
Protocol procedure/ assessment	Any type								
	Incorrect version of ICF signed								

Table 4: Distribution of Protocol Deviations by Category, Type, and Treatment Group *(continued)*

Category	Deviation Type	Intradermal MVA-BN 2×10^7 (N=X)		Intradermal MVA-BN 1×10^7 (N=X)		Subcutaneous MVA-BN 1×10^8 (N=X)		All Participants (N=X)	
		Number of Participants	Number of Deviations	Number of Participants	Number of Deviations	Number of Participants	Number of Deviations	Number of Participants	Number of Deviations
	Blood not collected								
	Too few aliquots obtained								
	Specimen result not obtained								
	Required procedure not conducted								
	Required procedure done incorrectly								
	Study product temperature excursion								
	Specimen temperature excursion								
	Other								
Treatment administration	Any type								
	Required procedure done incorrectly								
	Study product temperature excursion								
	Other								

Note: N = Number of participants enrolled.

12.2.2 Displays of Adverse Events

Table 5: Solicited Adverse Event Grading Scale

Mild:	No interference with activity
Moderate:	Some interference with activity
Severe:	Prevents daily activity
Potentially Life Threatening:	ER visit or hospitalization
Note: If not otherwise specified in "*FDA Guidance for Industry, Toxicity Grading Scale for Healthy Adults and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials*"	

Table 6: Induration Grading Scale

Rule Type	Functional scale assessment (FA)	Measurement (MS)	Rule to Apply for Final Grading	Final Grade
Standard tox table	0 or 1	<2.5cm	**Rule 1:** FA = 0 or 1 AND MS < 2.5cm	None
	1	2.5-5cm	**Rule 2:** FA =1 AND MS 2.5-5cm	1
	2	5.1-10cm	**Rule 3:** FA = 2 OR MS 5.1-10cm	2
	3	>10cm	**Rule 4:** FA = 3 OR MS >10cm	3
	4	Any	**Rule 5:** FA = 4 OR Necrosis associated with induration or both induration and erythema	4
Graded MS, FA None	0	2.5-5cm	Rule 1	None
One assessment missing	0	Missing	N/A	None
	1	Missing	N/A	1
	Missing	2.5-5.0 cm	N/A	1
	2/3/4	Missing	Rules 3,4,5	2/3/4
	Missing	<2.5cm	N/A	None
	Missing	5.1-10cm/>10cm	Rules 3,4	2/3
One assessment marked "not done"	0	Not Done	N/A	None
	1	Not Done	N/A	1
	2/3/4	Not Done	Rules 3,4,5	2/3/4
	Not Done	<2.5cm	N/A	None
	Not Done	2.5-5cm	N/A	1
	Not Done	5.1-10cm/>10cm	Rules 3,4	2/3
Two Assessments Missing/ Not Done	Missing	Missing	N/A	Missing
	Not Done	Not Done	N/A	Not Done

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Not applicable.

14.1 Description of Study Participants

14.1.1 Disposition of Participants

Table 7: Participant Disposition by Treatment Group

Participant Disposition	Intradermal MVA-BN 2×10^7 (N=X)		Intradermal MVA-BN 1×10^7 (N=X)		Subcutaneous MVA-BN 1×10^8 (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%
Screened	--	--	--	--	--	--	x	--
Enrolled/Randomized	x	100	x	100	x	100	x	100
Received Dose 1	x	Xx	x	xx	x	xx	x	xx
Received Dose 2[a]	x	Xx	x	xx	x	xx	x	xx
Completed Primary Endpoint (Day 43)								
Completed Final Blood Draw (Study Day 365)								
Completed Follow-up (Study Day 365)[a]								
Completed Day 365 Per Protocol[b]								

Notes: N = Number of participants enrolled.

n = Number of participants meeting the row criteria.

[a] Refer to Listing 2 for reasons participants discontinued or terminated early.

[b] Refer to Listing 5 for reasons participants are excluded from the Analysis populations.

Table 8: Analysis Populations by Treatment Group

Analysis Populations	Reason Participants Excluded	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
		n	%	N	%	n	%	%	n
Safety Population	Did not receive study product	x	xx	X	xx	x	xx	x	xx
mITT Population	Any Reason								
	Did not receive study product								
	No pre-vaccination sample with results reported								
	No post-vaccination sample with results reported								
Per Protocol Population, All Days	Any Reason								
	Did not receive study product								
	No pre-vaccination sample with results reported								
	No post-vaccination sample with results reported								
	Ineligible at baseline								
Per Protocol Population, Day 1	Major protocol deviation								
	Visit substantially out of window								
Per Protocol Population, Day 15	Major protocol deviation								
	Visit substantially out of window								
Per Protocol Population, Day 29	Major protocol deviation								
	Visit substantially out of window								
Per Protocol Population, Day 43	Major protocol deviation								
	Visit substantially out of window								
Per Protocol Population, Day 57	Major protocol deviation								
	Visit substantially out of window								
Per Protocol Population, Day 90	Major protocol deviation								

Table 8: Analysis Populations by Treatment Group *(continued)*

Analysis Populations	Reason Participants Excluded	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
		n	%	N	%	n	%	%	n
	Visit substantially out of window								
Per Protocol Population, Day 181	Major protocol deviation								
	Visit substantially out of window								
Per Protocol Population, Day 365	Major protocol deviation								
	Visit substantially out of window								

Notes: N = Number of participants enrolled.
n = Number of participants meeting row criteria.

Table 9: Dates of First Treatment by Site and Treatment Group

Treatment Group	Dates of Dosing	Total (Entire period of enrollment)	09SEP2022-15SEP2022	16SEP2022-22SEP2022	23SEP2022-29SEP2022	30SEP2022-06OCT2022	07OCT2022-14OCT2022
Intradermal MVA-BN 2 x 10^7	Saint Louis University	x	x	X	x	x	x
	Hope Clinic of the Emory Vaccine Center						
	Baylor College of Medicine						
	Vanderbilt University						
	UC San Diego						
	George Washington University						
	NIH Clinical Research Center						
	Brigham & Women's Hospital						
	All Sites						
Intradermal MVA-BN 1 x 10^7	Saint Louis University						
	Hope Clinic of the Emory Vaccine Center						
	Baylor College of Medicine						
	Vanderbilt University						
	UC San Diego						
	George Washington University						
	NIH Clinical Research Center						
	Brigham & Women's Hospital						
	All Sites						
Subcutaneous MVA-BN 1 x 10^8	Saint Louis University						
	Hope Clinic of the Emory Vaccine Center						
	Baylor College of Medicine						

Table 9: Dates of First Treatment by Site and Treatment Group *(continued)*

Treatment Group	Dates of Dosing	Total (Entire period of enrollment)	09SEP2022-15SEP2022	16SEP2022-22SEP2022	23SEP2022-29SEP2022	30SEP2022-06OCT2022	07OCT2022-14OCT2022
	Vanderbilt University						
	UC San Diego						
	George Washington University						
	NIH Clinical Research Center						
	Brigham & Women's Hospital						
	All Sites						
All Treatment Groups	Saint Louis University						
	Hope Clinic of the Emory Vaccine Center						
	Baylor College of Medicine						
	Vanderbilt University						
	UC San Diego						
	George Washington University						
	NIH Clinical Research Center						
	Brigham & Women's Hospital						
	All Sites						

Table 10: Ineligibility Summary of Screen Failures

Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of participants failing any eligibility criterion	x	100
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx
Eligible But Not Enrolled	N/A	x	N/A

[a] More than one criterion may be marked per participant.
[b] Denominator for percentages is the total number of screen failures.

14.1.2 Demographic Data by Study Group

Table 11: Summary of Categorical Demographic and Baseline Characteristics by Site

Variable	Characteristic	Saint Louis University (N=X)		Hope Clinic of the Emory Vaccine Center (N=X)		Baylor College of Medicine (N=X)		Vanderbilt University (N=X)		UC San Diego (N=X)		George Washington University (N=X)		NIH Clinical Research Center (N=X)		Brigham & Women's Hospital (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	N	%	n	%	n	%	n	%	n	%	n	%
Sex Assigned at Birth	Male	x	xx	x	xx	x	xx	X	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Female																		
	Intersex																		
	Not Reported																		
Gender Identity	Cisgender Man	x	xx	x	xx	x	xx	X	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Cisgender Woman																		
	Genderqueer																		
	Gender Non-binary																		
	Gender Non-conforming																		
	Transgender Man/Trans Man																		
	Transgender Woman/Trans Woman																		
	Other																		
	Decline to state																		
Sexual Identity	Heterosexual or straight	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Lesbian or gay																		
	Bisexual																		
	Queer																		

Table 11: Summary of Categorical Demographic and Baseline Characteristics by Site *(continued)*

Variable	Characteristic	Saint Louis University (N=X)		Hope Clinic of the Emory Vaccine Center (N=X)		Baylor College of Medicine (N=X)		Vanderbilt University (N=X)		UC San Diego (N=X)		George Washington University (N=X)		NIH Clinical Research Center (N=X)		Brigham & Women's Hospital (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	N	%	n	%	n	%	n	%	n	%	n	%
	Pansexual																		
	Asexual																		
	Other																		
	Decline to state																		
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino																		
	Not Reported																		
	Unknown																		
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian																		
	Native Hawaiian or Other Pacific Islander																		
	Black or African American																		
	White																		
	Multi-Racial																		
	Unknown																		
HIV Status	Negative	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Positive																		

Note: N = Number of participants enrolled.
n = Number of participants meeting the row criteria.

Table 12: Summary of Continuous Demographic and Baseline Characteristics by Site

Variable	Statistic	Saint Louis University (N=X)	Hope Clinic of the Emory Vaccine Center (N=X)	Baylor College of Medicine (N=X)	Vanderbilt University (N=X)	UC San Diego (N=X)	George Washington University (N=X)	NIH Clinical Research Center (N=X)	Brigham & Women's Hospital (N=X)	All Participants (N=X)
Age	Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Minimum	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x
Note: N = Number of participants enrolled.										

Table 13: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group

Variable	Characteristic	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx	x	xx
	Female								
	Intersex								
	Not Reported								
Gender Identity	Cisgender Man	x	xx	x	xx	x	xx	x	xx
	Cisgender Woman								
	Genderqueer								
	Gender Non-binary								
	Gender Non-conforming								
	Transgender Man/Trans Man								
	Transgender Woman/Trans Woman								
	Other								
	Decline to state								
Sexual Identity	Heterosexual or straight	x	xx	x	xx	x	xx	x	xx
	Lesbian or gay								
	Bisexual								
	Queer								
	Pansexual								
	Asexual								
	Other								
	Decline to state								
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino								
	Not Reported								
	Unknown								
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx
	Asian								
	Native Hawaiian or Other Pacific Islander								
	Black or African American								
	White								
	Multi-Racial								
	Unknown								

Table 13: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group *(continued)*

Variable	Characteristic	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%
HIV Status	Negative	x	xx	x	xx	x	xx	x	xx
	Positive								

Note: N = Number of participants enrolled.
n = Number of participants meeting the row criteria.

Table 14: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group

Variable	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)	All Participants (N=X)
Age (years)	Mean	xx.x	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx,x	xx,x	xx,x
	Median	x	x	x	x
	Minimum	x	x	x	x
	Maximum	x	x	x	x
Note: N = Number of participants enrolled.					

14.1.3 Prior and Concurrent Medical Conditions

Table 15: Summary of Participants with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group

MedDRA System Organ Class	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx	x	xx
[SOC 1]								
[SOC 2]								

Notes: N = Number of participants in the Safety Population.
n = Number of participants reporting medical history within the specified SOC. A participant is only counted once per SOC.

14.2 Immunogenicity Data

Table 16: Primary Hypothesis Testing, mITT Population

Hypothesis	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
At Day 43 the humoral immune response non-inferior to the standard 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	N/A
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A

Notes: N = Number of participants in the mITT Population.
n = Number of participants with data at timepoint.
GMT = Geometric mean titer.
GMTR = Geometric mean titer ratio.
[a] Two-sample t-test with unequal variance, noninferiority (NI) margin of 0.5 and two-sided type I error rate of 0.05.
[b] If the lower bound of the GMTR 95% CI is greater than or equal to 0.5 (minus 0.301 on the log10 scale), the result is "Yes".

Table with similar format:

Table 17: Primary Hypothesis Testing, Per Protocol Population

Table 18: Vaccinia virus specific PRNT Secondary Hypothesis Testing, mITT Population

Hypothesis	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
At Day 365 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A
At Day 1 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A
At Day 15 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A
At Day 29 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A

Table 18: Vaccinia virus specific PRNT Secondary Hypothesis Testing, mITT Population *(continued)*

Hypothesis	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
	Non-inferiority result[b]	Yes or No	Yes or No	N/A
At Day 57 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A
At Day 90 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A
At Day 181 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A
At peak (any day post-dose 1) humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Vaccinia specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

Table 18: Vaccinia virus specific PRNT Secondary Hypothesis Testing, mITT Population *(continued)*

Hypothesis	Statistic	Intradermal MVA-BN 2×10^7 (N=X)	Intradermal MVA-BN 1×10^7 (N=X)	Subcutaneous MVA-BN 1×10^8 (N=X)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A

Notes: N = Number of participants in the mITT Population.
n = Number of participants with data at timepoint.
GMT = Geometric mean titer.
GMTR = Geometric mean titer ratio.
[a] Two-sample t-test with unequal variance, noninferiority (NI) margin of 0.5 and two-sided type I error rate of 0.05.
[b] If the lower bound of the GMTR 95% CI is greater than or equal to 0.5 (minus 0.301 on the log10 scale), the result is "Yes".

Table with similar format:

Table 19: Vaccinia virus specific PRNT Secondary Hypothesis Testing, Per Protocol Population

Table 20: Vaccinia specific PRNT Half-Life Secondary Hypothesis Testing, mITT Population

Hypothesis	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
Humoral immune responses as assessed by Vaccinia specific PRNT half-life similar to 1 x 10^8 MVA-BN SC regimen	n	x	x	x
	Mean half-life (days)	xx	xx	xx
	Min, Max	xx, xx	xx, xx	xx, xx
	p-value[a]	x.xxx	x.xxx	N/A

Notes: N = Number of participants in the mITT Population.
n = Number of participants with data.
[a] Wilcoxon-Mann-Whitney test

Table with similar format:

Table 21: Vaccinia specific PRNT Half-Life Secondary Hypothesis Testing, Per Protocol Population

Table 22: Monkeypox virus specific PRNT Hypothesis Testing, mITT Population

Hypothesis	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
At Day 1 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Monkeypox specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A
At Day 43 humoral immune response non-inferior to 1 x 10^8 MVA-BN SC regimen, as assessed by Monkeypox specific PRNT GMT	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	p-value[a]	x.xxx	x.xxx	N/A
	Non-inferiority result[b]	Yes or No	Yes or No	N/A

Notes: N = Number of participants in the mITT Population.
n = Number of participants with data at timepoint.
GMT = Geometric mean titer.
GMTR = Geometric mean titer ratio.
[a] Two-sample t-test with unequal variance, noninferiority (NI) margin of 0.5 and two-sided type I error rate of 0.05.
[b] If the lower bound of the GMTR 95% CI is greater than or equal to 0.5 (minus 0.301 on the log10 scale), the result is "Yes".

Table with similar format:

Table 23: Monkeypox virus specific PRNT Hypothesis Testing, Per Protocol Population

Table 24: Vaccinia virus specific PRNT Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Population

Time Point	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
Study Day 1, Pre-Dose 1	n	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Study Day 15, Post Dose 1	n			
	GMT (95% CI)			
Study Day 29, Pre-Dose 2	n			
	GMT (95% CI)			
Study Day 43, Post Dose 2	n			
	GMT (95% CI)			
Study Day 57, Post Dose 2	n			
	GMT (95% CI)			
Study Day 90, Post Dose 2	n			
	GMT (95% CI)			
Study Day 181, Post Dose 2	n			
	GMT (95% CI)			
Study Day 365, Post Dose 2	n			
	GMT (95% CI)			
Peak Anytime Post Dose 1	n			
	GMT (95% CI)			

Notes: N = Number of participants in the mITT Population.
n = Number of participants with data at timepoint.
GMT = Geometric Mean Titer.
CI = Confidence Interval.

Tables with similar format:

Table 25: Vaccinia virus specific PRNT Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, Per Protocol Population

Table 26: Monkeypox virus specific PRNT Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Population

Table 27: Monkeypox virus specific PRNT Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, Per Protocol Population

Table 28: Anti-MVA Neutralizing Antibody Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Population

Table 32: Vaccinia virus specific PRNT Geometric Mean Titer Ratio (GMTR) to Subcutaneous MVA-BN 1 x 10^8 Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Population

Time Point	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)
Study Day 1, Pre-Dose 1	n	x	x
	GMTR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
Study Day 15, Post Dose 1	n		
	GMTR (95% CI)		
Study Day 29, Pre-Dose 2	n		
	GMTR (95% CI)		
Study Day 43, Post Dose 2	n		
	GMTR (95% CI)		
Study Day 57, Post Dose 2	n		
	GMTR (95% CI)		
Study Day 90, Post Dose 2	n		
	GMTR (95% CI)		
Study Day 181, Post Dose 2	n		
	GMTR (95% CI)		
Study Day 365, Post Dose 2	n		
	GMTR (95% CI)		
Peak Anytime Post Dose 1	n		
	GMTR (95% CI)		

Notes: N = Number of participants in the mITT Population.
n = Number of participants with data at timepoint.
GMTR = Geometric Mean Titer Ratio.
CI = Confidence Interval. The CI will be calculated using Student's t distribution.

Tables with similar format:

Table 33: Vaccinia virus specific PRNT Geometric Mean Titer Ratio (GMTR) to Subcutaneous MVA-BN 1 x 10^8 Results with 95% Confidence Intervals by Time Point and Treatment Group, Per Protocol Population

Table 34: Monkeypox virus specific PRNT Geometric Mean Titer Ratio (GMTR) to Subcutaneous MVA-BN 1 x 10^8 Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Population

Table 35: Monkeypox virus specific PRNT Geometric Mean Titer Ratio (GMTR) to Subcutaneous MVA-BN 1 x 10^8 Results with 95% Confidence Intervals by Time Point and Treatment Group, Per Protocol Population

Table 36: Vaccinia virus specific PRNT Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, mITT Population

Time Point	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
Study Day 15, Post Dose 1	n	x	x	x
	GMFR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	% with Seroconversion[b] (95% CI)	x (x, x)	x (x, x)	x (x, x)
Study Day 29, Pre-Dose 2	n			
	GMFR[a] (95% CI)			
	% with Seroconversion[b] (95% CI)			
Study Day 43, Post Dose 2	n			
	GMFR[a] (95% CI)			
	% with Seroconversion[b] (95% CI)			
Study Day 57, Post Dose 2	n			
	GMFR[a] (95% CI)			
	% with Seroconversion[b] (95% CI)			
Study Day 90, Post Dose 2	n			
	GMFR[a] (95% CI)			
	% with Seroconversion[b] (95% CI)			
Study Day 181, Post Dose 2	n			
	GMFR[a] (95% CI)			
	% with Seroconversion[b] (95% CI)			
Study Day 365, Post Dose 2	n			
	GMFR[a] (95% CI)			
	% with Seroconversion[b] (95% CI)			
Peak Anytime Post Dose 1	n			
	GMFR[a] (95% CI)			

Table 36: Vaccinia virus specific PRNT Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, mITT Population *(continued)*

Time Point	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
	% with Seroconversion[b] (95% CI)			

Notes: N = Number of participants in the mITT Population.
n = Number of participants with data at timepoint.
CI = Confidence Interval.
[a] GMFR represents the geometric mean fold rise in antibody for the corresponding time point compared to pre-dose 1.
[b] Seroconversion represents the percentage of subjects with at least a 2-Fold Rise in antibody compared to pre-dose 1 if any positive at pre-dose 1 or any positive if negative at pre-dose 1.

Tables with similar format:

Table 37: Vaccinia virus specific PRNT Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, Per Protocol Population

Table 38: Monkeypox virus specific PRNT Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, mITT Population

Table 39: Monkeypox virus specific PRNT Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, Per Protocol Population

Table 40: Anti-MVA Neutralizing Antibody Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, mITT Population

Table 41: Anti-MVA Neutralizing Antibody Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, Per Protocol Population

Table 42: Anti-MPXV clade I Neutralizing Antibody Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, mITT Population

Table 43: Anti-MPXV clade I Neutralizing Antibody Geometric Mean Fold Rise (GMFR) and Seroconversion by Time Point and Treatment Group, Per Protocol Population

Table 44: Ratio of Monkeypox virus specific PRNT Geometric Mean Titer (GMT) to Vaccinia virus specific PRNT Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Population

Time Point	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
Study Day 1, Pre-Dose 1	n	x	x	x
	GMT Ratio (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Study Day 43, Post Dose 2	n			
	GMT Ratio (95% CI)			
Notes: N = Number of participants in the mITT Population. n = Number of participants with data at timepoint. GMT Ratio = Monkeypox virus specific PRNT Geometric Mean Titer/Vaccinia virus specific PRNT Geometric Mean Titer CI = Confidence Interval.				

Table with similar format:

Table 45: Ratio of Monkeypox virus specific PRNT Geometric Mean Titer (GMT) to Vaccinia virus specific PRNT Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, Per Protocol Population

Table 46: Ratio of Monkeypox virus specific PRNT Geometric Meant Fold Rise (GMFR) to Vaccinia virus specific PRNT Geometric Mean Fold Rise (GMFR) by Time Point and Treatment Group, mITT Population

Time Point	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
Study Day 43, Post Dose 2	n	x	x	x
	GMFR Ratio[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

Notes: N = Number of participants in the mITT Population.

n = Number of participants with data at timepoint.

CI = Confidence Interval.

[a] GMFR Ratio represents the geometric mean fold rise in Monkeypox virus specific antibody compared to pre-dose 1 divided by the geometric mean fold rise in Vaccinia virus specific antibody compared to pre-dose 1

Table with similar format:

Table 47: Ratio of Monkeypox virus specific PRNT Geometric Meant Fold Rise (GMFR) to Vaccinia virus specific PRNT Geometric Mean Fold Rise (GMFR) by Time Point and Treatment Group, Per Protocol Population

Table 48: Immunogenicity Correlations at Day 43 by Treatment Group, mITT Population

Assay	Spearman Correlation (95% CI)			
	Intradermal MVA-BN 2 x 10^7 (N=X)	**Intradermal MVA-BN 1 x 10^7** (N=X)	**Subcutaneous MVA-BN 1 x 10^8** (N=X)	**All Participants** (N=X)
Vaccinia virus specific PRNT GMFR vs Monkeypox virus specific PRNT GMFR	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)
Vaccinia virus specific PRNT GMFR vs Anti-MVA Neutralizing Antibody GMFR	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)
Vaccinia virus specific PRNT GMFR vs Anti-MPXV clade I Neutralizing Antibody GMFR	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)	x.xx (x.xxx-x.xxx)

Table with similar format:

Table 49: Immunogenicity Correlations at Day 43 by Treatment Group, Per Protocol Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 50: Summary of Secondary Safety Outcome

	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)		p-value[c]	p-value[d]
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**		
At least one Grade 3 or 4 solicited local or systemic AE	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x.xxx**	**x.xxx**
At least one related unsolicited AE	x	x	x	x	x	x	x	x	x.xxx	x.xxx
At least one related unsolicited SAE[b]	x	x	x	x	x	x	x	x	x.xxx	x.xxx
At least one related unsolicited MAAE	x	x	x	x	x	x	x	x	x.xxx	x.xxx
Withdrawal from study	x	x	x	x	x	x	x	x	x.xxx	x.xxx
Discontinuation of treatment	x	x	x	x	x	x	x	x	x.xxx	x.xxx

Notes: N = Number of participants in the Safety Population.
n = Number of participants meeting the row criteria.
[a] Participants are counted once for each category regardless of the number of events.
[b] A listing of Serious Adverse Events is included in Table 78.
[c] Fisher's exact test, Intradermal MVA-BN 2 x 10^7 vs. Subcutaneous MVA-BN 1 x 10^8.
[d] Fisher's exact test, Intradermal MVA-BN 1 x 10^7 vs. Subcutaneous MVA-BN 1 x 10^8.

Table 51: Overall Summary of Adverse Events

	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one local solicited adverse event	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event	x	x	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x	x	x
At least one related unsolicited adverse event	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x
Life-threatening (Grade 4)								
Not yet assessed								
At least one Grade 3 or Grade 4 unsolicited adverse event	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x
At least one serious adverse event[b]	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x
At least one adverse event leading to study withdrawal [c]	x	x	x	x	x	x	x	x
At least one adverse event leading to discontinuation of study product[c]	x	x	x	x	x	x	x	x
At least one medically attended adverse event	x	x	x	x	x	x	x	x

Table 51: Overall Summary of Adverse Events *(continued)*

	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one unanticipated problem	x	x	x	x	x	x	x	x
At least one suspected unexpected serious adverse reaction	x	x	x	x	x	x	x	x

Notes: N = Number of participants in the Safety Population.

n = Number of participants meeting the row criteria.

[a] Participants are counted once for each category regardless of the number of events.

[b] A listing of Serious Adverse Events is included in Table 78.

[c] As reported on the Adverse Event eCRF.

Table 52: Adverse Events Occurring in 5% of Participants in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - Safety Population

Preferred Term	MedDRA System Organ Class	Intradermal MVA-BN 2 x 10^7 (N=X)			Intradermal MVA-BN 1 x 10^7 (N=X)			Subcutaneous MVA-BN 1 x 10^8 (N=X)			All Participants (N=X)		
		n	%	Events	n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events													
All	All	x	x	x	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.												
Other (Non-serious) Adverse Events													
All	All	x	x	x	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.												

N = Number of participants in the Safety Population (number of participants at risk).
n = Number of participants reporting event.
Events = Total frequency of events reported.

14.3.1.1 Solicited Adverse Events

Table 53: Number and Percentage of Participants Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Dose, and Treatment Group

Symptom	Post Dose 1 Intradermal MVA-BN 2 x 10^7 (N=X)			Post Dose 1 Intradermal MVA-BN 1 x 10^7 (N=X)			Post Dose 1 Subcutaneous MVA-BN 1 x 10^8 (N=X)			Post Dose 2 Intradermal MVA-BN 2 x 10^7 (N=X)			Post Dose 2 Intradermal MVA-BN 1 x 10^7 (N=X)			Post Dose 2 Subcutaneous MVA-BN 1 x 10^8 (N=X)			Post Either Dose Intradermal MVA-BN 2 x 10^7 (N=X)			Post Either Dose Intradermal MVA-BN 1 x 10^7 (N=X)			Post Either Dose Subcutaneous MVA-BN 1 x 10^8 (N=X)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Symptom	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
Any Systemic Symptom																													
Fever																													
Chills																													
Nausea																													
Headache																													
Fatigue																													
Change in appetite																													
Myalgia																													
Arthralgia																													
Any Local Symptom																													

Table 53: Number and Percentage of Participants Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Dose, and Treatment Group *(continued)*

Symptom	Post Dose 1 Intradermal MVA-BN 2 x 10^7 (N=X)			Post Dose 1 Intradermal MVA-BN 1 x 10^7 (N=X)			Post Dose 1 Subcutaneous MVA-BN 1 x 10^8 (N=X)			Post Dose 2 Intradermal MVA-BN 2 x 10^7 (N=X)			Post Dose 2 Intradermal MVA-BN 1 x 10^7 (N=X)			Post Dose 2 Subcutaneous MVA-BN 1 x 10^8 (N=X)			Post Either Dose Intradermal MVA-BN 2 x 10^7 (N=X)			Post Either Dose Intradermal MVA-BN 1 x 10^7 (N=X)			Post Either Dose Subcutaneous MVA-BN 1 x 10^8 (N=X)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Pain at injection site																													
Erythema/redness																													
Induration/swelling[a]																													
Pruritis at injection site																													

Notes: N = Number of participants in the Safety Population.

n = Number of participants meeting the row criteria.

CI = Confidence interval, calculated using Clopper-Pearson methodology.

[a] Graded according to Table 6.

Table 54: Comparison of the Proportion of Participants Experiencing Solicited Events Post Either Dose by Treatment Group

Symptom	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
Any Symptom	n	xx	xx	xx
	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	N/A (Reference Level)
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)	N/A (Reference Level)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Any Systemic Symptom	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Fever	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Chills	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Nausea	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Headache	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Fatigue	n			

Table 54: Comparison of the Proportion of Participants Experiencing Solicited Events Post Either Dose by Treatment Group *(continued)*

Symptom	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Change in appetite	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Myalgia	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Arthralgia	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Any Local Symptom	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Pain at injection site	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Erythema/redness	n			
	Proportion (95% CI)			

Table 54: Comparison of the Proportion of Participants Experiencing Solicited Events Post Either Dose by Treatment Group *(continued)*

Symptom	Statistic	Intradermal MVA-BN 2 x 10^7 (N=X)	Intradermal MVA-BN 1 x 10^7 (N=X)	Subcutaneous MVA-BN 1 x 10^8 (N=X)
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Induration/swelling	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			
Pruritis at injection site	n			
	Proportion (95% CI)			
	Difference from Subcutaneous MVA-BN 1 x 10^8 (95% CI)			
	Difference from Intradermal MVA-BN 2 x 10^7 (95% CI)			

Notes: N = Number of participants in the Safety Population who received at least one dose.
n = Number of participants meeting the row criteria.
Proportion = n divided by N
CI = Confidence Interval, calculated using Clopper-Pearson methodology.

Table 55: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, and Dose – Intradermal MVA-BN 2 x 10^7

Symptom	Severity	Post Dose 1 (N=X)			Post Dose 2 (N=X)			Post Either Dose (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Symptoms										
Any Symptom	None	x	xx		x	xx		x	xx	
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Systemic Symptoms										
Any Systemic Symptom	None	x	xx		x	xx		x	xx	
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Fever	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Chills	None									
	Mild									
	Moderate									
	Severe									

Table 55: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose – Intradermal MVA-BN 2 x 10^7 *(continued)*

Symptom	Severity	Post Dose 1 (N=X)			Post Dose 2 (N=X)			Post Either Dose (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
	Life-Threatening									
Nausea	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Headache	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Fatigue	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Change in appetite	None									
	Mild									
	Moderate									
	Severe									

Table 55: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose – Intradermal MVA-BN 2 x 10^7 *(continued)*

Symptom	Severity	Post Dose 1 (N=X)			Post Dose 2 (N=X)			Post Either Dose (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
	Life-Threatening									
Myalgia	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Arthralgia	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Local Symptoms										
Any Local Symptom	None	x	xx		x	xx		x	xx	
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Pain at injection site	None									
	Mild									
	Moderate									
	Severe									

Table 55: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose – Intradermal MVA-BN 2 x 10^7 *(continued)*

Symptom	Severity	Post Dose 1 (N=X)			Post Dose 2 (N=X)			Post Either Dose (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
	Life-Threatening									
Erythema/redness	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Induration/swelling	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									
Pruritis at injection site	None									
	Mild									
	Moderate									
	Severe									
	Life-Threatening									

Notes: N = Number of participants in the Safety Population who received the specified dose. Severity is the maximum severity reported post dosing for each participant for each day.

n = Number of participants meeting the row criteria.

CI = Confidence interval, calculated using Clopper-Pearson methodology.

Tables with similar format:

Table 56: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, and Dose – Intradermal MVA-BN 1 x 10^7

Table 57: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, and Dose – Subcutaneous MVA-BN 1 x 10^8

Table 58: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 1-8 (N=X)

Symptom	Severity	Pre-Dose 1		Post Dose 1		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Systemic Symptoms																					
Any Systemic Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Fever	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				

Table 58: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X) *(continued)*

Symptom	Severity	Pre-Dose 1		Post Dose 1		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Chills	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Nausea	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Headache	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Fatigue	None																				
	Mild																				
	Moderate																				
	Severe																				

Table 58: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X) *(continued)*

Symptom	Severity	Pre-Dose 1		Post Dose 1		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Life-Threatening																				
	Not Reported																				
Change in appetite	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Myalgia	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Arthralgia	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Local Symptoms																					

Table 58: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X) *(continued)*

Symptom	Severity	Pre-Dose 1		Post Dose 1		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Local Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Pain at injection site	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Erythema/ redness	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Induration/ swelling	None																				

Table 58: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X) *(continued)*

Symptom	Severity	Pre-Dose 1		Post Dose 1		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				
Pruritis at injection site	None																				
	Mild																				
	Moderate																				
	Severe																				
	Life-Threatening																				
	Not Reported																				

Notes: N = Number of participants in the Safety Population who received the specified dose. Severity is the maximum severity reported post dosing for each participant for each day.

n = Number of participants meeting the row criteria.

Table 59: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X)

Symptom	Severity	Day 9		Day 10		Day 11		Day 12		Day 13		Day 14		Day 15		Any Post Dose 1[a]	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Systemic Symptoms																	
Any Systemic Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Fever	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																

Table 59: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X) *(continued)*

Symptom	Severity	Day 9		Day 10		Day 11		Day 12		Day 13		Day 14		Day 15		Any Post Dose 1[a]	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Chills	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Nausea	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Headache	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Fatigue	None																
	Mild																
	Moderate																

Table 59: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X) *(continued)*

Symptom	Severity	Day 9		Day 10		Day 11		Day 12		Day 13		Day 14		Day 15		Any Post Dose 1[a]	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Severe																
	Life-Threatening																
	Not Reported																
Change in appetite	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Myalgia	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Arthralgia	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																

Table 59: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X) *(continued)*

Symptom	Severity	Day 9		Day 10		Day 11		Day 12		Day 13		Day 14		Day 15		Any Post Dose 1[a]	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Local Symptoms																	
Any Local Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Pain at injection site	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Erythema/ redness	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																

Table 59: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Intradermal MVA-BN 2 x 10^7, Post Dose 1 Days 9-15 (N=X) *(continued)*

Symptom	Severity	Day 9		Day 10		Day 11		Day 12		Day 13		Day 14		Day 15		Any Post Dose 1[a]	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Induration/ swelling	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																
Pruritis at injection site	None																
	Mild																
	Moderate																
	Severe																
	Life-Threatening																
	Not Reported																

Notes: N = Number of participants in the Safety Population who received the specified dose. Severity is the maximum severity reported post dosing for each participant for each day.

n = Number of participants meeting the row criteria.

[a] Indicates how many participants had "None", "Mild", "Moderate", "Severe", "Life-Threatening", or "Not Reported" for any day. A participant may be counted in more than one of these categories.

Tables with similar format:

Table 60: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group - Intradermal MVA-BN 2 x 10^7, Post Dose 2 Days 1-8 (N=X)

Table 61: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group - Intradermal MVA-BN 2 x 10^7, Post Dose 2 Days 9-15 (N=X)

Table 62: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group - Intradermal MVA-BN 1 x 10^7, Post Dose 1 Days 1-8 (N=X)

Table 63: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group - Intradermal MVA-BN 1 x 10^7, Post Dose 1 Days 9-15 (N=X)

Table 64: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group - Intradermal MVA-BN 1 x 10^7, Post Dose 2 Days 1-8 (N=X)

Table 65: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group - Intradermal MVA-BN 1 x 10^7, Post Dose 2 Days 9-15 (N=X)

Table 66: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group – Subcutaneous MVA-BN 1 x 10^8, Post Dose 1 Days 1-8 (N=X)

Table 67: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group – Subcutaneous MVA-BN 1 x 10^8, Post Dose 1 Days 9-15 (N=X)

Table 68: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group – Subcutaneous MVA-BN 1 x 10^8, Post Dose 2 Days 1-8 (N=X)

Table 69: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Severity, Dose, Day Post Dosing, and Treatment Group – Subcutaneous MVA-BN 1 x 10^8, Post Dose 2 Days 9-15 (N=X)

Table 70: Number and Percentage of Participants Experiencing Solicited Events for Dose 1 Compared with Dose 2 by Treatment Group

Treatment Group		Dose 2 – Participants with No Symptoms	Dose 2 – Participants with Mild or Greater Symptoms	Dose 2 – Total Number of Participants
Any Symptoms				
Intradermal MVA-BN 2 x 10^7	Dose 1 – Participants with No Symptoms	n/N (%)	n/N (%)	n/N (%)
	Dose 1 – Participants with Mild or Greater Symptoms	n/N (%)	n/N (%)	n/N (%)
	Dose 1 – Total Number of Participants with Data	n/N (%)	n/N (%)	n/N (%)
Intradermal MVA-BN 1 x 10^7	Dose 1 – Participants with No Symptoms			
	Dose 1 – Participants with Mild or Greater Symptoms			
	Dose 1 – Total Number of Participants with Data			
Subcutaneous MVA-BN 1 x 10^8	Dose 1 – Participants with No Symptoms			
	Dose 1 – Participants with Mild or Greater Symptoms			
	Dose 1 – Total Number of Participants with Data			
Systemic Symptoms				
Intradermal MVA-BN 2 x 10^7	Dose 1 – Participants with No Symptoms	n/N (%)	n/N (%)	n/N (%)
	Dose 1 – Participants with Mild or Greater Symptoms	n/N (%)	n/N (%)	n/N (%)
	Dose 1 – Total Number of Participants with Data	n/N (%)	n/N (%)	n/N (%)
Intradermal MVA-BN 1 x 10^7	Dose 1 – Participants with No Symptoms			
	Dose 1 – Participants with Mild or Greater Symptoms			

Table 70: Number and Percentage of Participants Experiencing Solicited Events for Dose 1 Compared with Dose 2 by Treatment Group *(continued)*

Treatment Group		Dose 2 – Participants with No Symptoms	Dose 2 – Participants with Mild or Greater Symptoms	Dose 2 – Total Number of Participants
	Dose 1 – Total Number of Participants with Data			
Subcutaneous MVA-BN 1 x 10^8	Dose 1 – Participants with No Symptoms			
	Dose 1 – Participants with Mild or Greater Symptoms			
	Dose 1 – Total Number of Participants with Data			
Local Symptoms				
Intradermal MVA-BN 2 x 10^7	Dose 1 – Participants with No Symptoms	n/N (%)	n/N (%)	n/N (%)
	Dose 1 – Participants with Mild or Greater Symptoms	n/N (%)	n/N (%)	n/N (%)
	Dose 1 – Total Number of Participants with Data	n/N (%)	n/N (%)	n/N (%)
Intradermal MVA-BN 1 x 10^7	Dose 1 – Participants with No Symptoms			
	Dose 1 – Participants with Mild or Greater Symptoms			
	Dose 1 – Total Number of Participants with Data			
Subcutaneous MVA-BN 1 x 10^8	Dose 1 – Participants with No Symptoms			
	Dose 1 – Participants with Mild or Greater Symptoms			
	Dose 1 – Total Number of Participants with Data			

Notes: N = number of participants in the Safety Population who received the first and second dose. [x] participants did not get the second dose and are not included in this table.
n = number of participants meeting the row criteria.

14.3.1.2 Unsolicited Adverse Events

Table 71: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Dose Number, and Treatment Group – Intradermal MVA-BN 2 x 10^7

MedDRA System Organ Class	MedDRA Preferred Term	Day 1-15 Post Dose 1 (N=X)				Day 16-29 Post Dose 1 (N=X)				Day 29-43 Post Dose 2 (N=X)				Day 44-181 Post Dose 2 (N=X)				Any Time Post Any Dose (N=X)			
		n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events
Any SOC	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
[SOC 1]	Any PT																				
	[PT 1]																				
	[PT 2]																				
[SOC 2]	Any PT																				
	[PT 1]																				
	[PT 2]																				

Notes: N = number of participants in the Safety Population who received the specified dose. This table presents number and percentage of participants and number of events. A participant is only counted once per PT/time point.

n = number of participants experiencing a given PT.

CI = confidence interval, calculated using Clopper-Pearson methodology.

Tables with similar format:

Table 72: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Dose Number, and Treatment Group – Intradermal MVA-BN 1 x 10^7

Table 73: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Dose Number, and Treatment Group – Subcutaneous MVA-BN 1 x 10^8

Table 74: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group

MedDRA System Organ Class	Preferred Term	Severity	Intradermal MVA-BN 2 x 10^7 (N = X)						Intradermal MVA-BN 1 x 10^7 (N = X)						Subcutaneous MVA-BN 1 x 10^8 (N = X)						All Participants (N = X)					
			Related		Not Related		Total		Related		Not Related		Total		Related		Not Related		Total		Related		Not Related		Total	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Life-Threatening	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
SOC 1	PT 1	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Life-Threatening	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	PT 2	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Life-Threatening	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: N = Number of participants in the Safety Population.
n = Number of participants meeting the row criteria.

Table 75: Related Unsolicited Adverse Events Within 15 Days Post Dosing by MedDRA System Organ Class and Preferred Term, Dose, and Treatment Group - Intradermal MVA-BN 2 x 10^7 (N=X)

		Day 1-15 Post Dose 1			Day 29-43 Post Dose 2			Within 15 Days Post Either Dose		
MedDRA System Organ Class	**MedDRA Preferred Term**	**n**	**%**	**Events**	**n**	**%**	**Events**	**n**	**%**	**Events**
Any SOC	Any PT	x	xx	x	x	xx	x	x	xx	x
[SOC 1]	Any PT									
	[PT 1]									
	[PT 2]									
[SOC 2]	Any PT									
	[PT 1]									
	[PT 2]									

Note: N = Number of participants in the Safety Population. This table presents number and percentage of participants and number of events. For each time point, a participant is only counted once per PT.

Tables with similar format:

Table 76: Related Unsolicited Adverse Events Within 15 Days Post Dosing by MedDRA System Organ Class and Preferred Term, Dose, and Treatment Group - Intradermal MVA-BN 1 x 10^7 (N=X)

Table 77: Related Unsolicited Adverse Events Within 15 Days Post Dosing by MedDRA System Organ Class and Preferred Term, Dose, and Treatment Group - Subcutaneous MVA-BN 1 x 10^8 (N=X)

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 78: Listing of Serious Adverse Events

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	SUSAR?	UP?	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Treatment Group: , AE Number:														
Comments:														
Participant ID: , Treatment Group: , AE Number:														
Comments:														

Table 79: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Treatment Group: , AE Number:										
Comments:										
Participant ID: , Treatment Group: , AE Number:										
Comments:										

Table 80: Listing of Other Significant Adverse Events

Adverse Event	Number of Doses Received at Time of Event	No. of Days Post Associated Dose	Duration of Event	Severity	MedDRA System Organ Class	MAAE?	UP?	Relationship	Outcome
Participant ID: , Treatment Group: , AE Number:									
Comments:									
Participant ID: , Treatment Group: , AE Number:									
Comments:									

Table 81: Duration of Injection Site AEs

	Injection Site Discoloration	Injection Site Erythema	Injection Site Induration	Injection Site Nodule	Injection Site Pain	Injection Site Pruritis
Pooled Intradermal Arms (MVA-BN 2 x 10^7 and MVA-BN 1 x 10^7) Post-Dose 1 (N=X)						
Any Severity (n)	x	x	x	x	x	x
Median Onset Day Post-Dose [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Median Days Duration [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Mild (n)	x	x	x	x	x	x
Median Onset Day Post-Dose [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Median Days Duration [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Moderate (n)	x	x	x	x	x	x
Median Onset Day Post-Dose [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Median Days Duration [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Severe (n)	x	x	x	x	x	x
Median Onset Day Post-Dose [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Median Days Duration [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Life-Threatening (n)	x	x	x	x	x	x
Median Onset Day Post-Dose [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Median Days Duration [Minimum, Maximum]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]	x [x, x]
Pooled Intradermal Arms (MVA-BN 2 x 10^7 and MVA-BN 1 x 10^7) Post-Dose 2 (N=X)						
Any Severity (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Mild (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Moderate (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						

Table 81: Duration of Injection Site AEs *(continued)*

	Injection Site Discoloration	Injection Site Erythema	Injection Site Induration	Injection Site Nodule	Injection Site Pain	Injection Site Pruritis
Median Days Duration [Minimum, Maximum]						
Severe (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Life-Threatening (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Subcutaneous MVA-BN 1 x 10^8 Post-Dose 1 (N=X)						
Any Severity (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Mild (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Moderate (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Severe (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Life-Threatening (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Subcutaneous MVA-BN 1 x 10^8 Post-Dose 2 (N=X)						
Any Severity (n)						

Table 81: Duration of Injection Site AEs *(continued)*

	Injection Site Discoloration	Injection Site Erythema	Injection Site Induration	Injection Site Nodule	Injection Site Pain	Injection Site Pruritis
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Mild (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Moderate (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Severe (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Life-Threatening (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
All Participants (N=X)						
Any Severity (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Mild (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Moderate (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Severe (n)						

Table 81: Duration of Injection Site AEs *(continued)*

	Injection Site Discoloration	Injection Site Erythema	Injection Site Induration	Injection Site Nodule	Injection Site Pain	Injection Site Pruritis
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						
Life-Threatening (n)						
Median Onset Day Post-Dose [Minimum, Maximum]						
Median Days Duration [Minimum, Maximum]						

Notes: N = number of participants in the Safety Population who received the specified dose.
n = number of participants experiencing a given PT.

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

(not included in SAP, but this is a placeholder for the CSR)

14.3.4 Abnormal Laboratory Value Listings (by Participant)

Not applicable.

14.3.5 Displays of Laboratory Results

Not applicable.

14.3.6 Displays of Vital Signs

Table 82: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Any Assessment

Time Point	Treatment Group	N	None		Mild		Moderate		Severe		Life-Threatening		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Intradermal MVA-BN 2 x 10^7	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Intradermal MVA-BN 1 x 10^7													
	Subcutaneous MVA-BN 1 x 10^8													
Day 29	Intradermal MVA-BN 2 x 10^7													
	Intradermal MVA-BN 1 x 10^7													
	Subcutaneous MVA-BN 1 x 10^8													
Max Severity Post Baseline	Intradermal MVA-BN 2 x 10^7													
	Intradermal MVA-BN 1 x 10^7													
	Subcutaneous MVA-BN 1 x 10^8													

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments.
N = Number of participants in the Safety Population with non-missing data at timepoint.
n = Number of participants experiencing the given severity.

Table 83: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Oral Temperature (°C)

Time Point	Treatment Group	N	None		Mild		Moderate		Severe		Life-Threatening		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Intradermal MVA-BN 2 x 10^7	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Intradermal MVA-BN 1 x 10^7													
	Subcutaneous MVA-BN 1 x 10^8													
Day 29	Intradermal MVA-BN 2 x 10^7													
	Intradermal MVA-BN 1 x 10^7													
	Subcutaneous MVA-BN 1 x 10^8													
Max Severity Post Baseline	Intradermal MVA-BN 2 x 10^7													
	Intradermal MVA-BN 1 x 10^7													
	Subcutaneous MVA-BN 1 x 10^8													

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments.
N = Number of participants in the Safety Population with non-missing data at timepoint.
n = Number of participants experiencing the given severity.

Table 84: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Diastolic Blood Pressure

Time Point	Treatment Group	N	None		Mild (Low)		Mild (High)		Moderate (Low)		Moderate (High)		Severe (Low)		Severe (High)		Life-Threatening (Low)		Life-Threatening (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Intradermal MVA-BN 2 x 10^7	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Intradermal MVA-BN 1 x 10^7																					
	Subcutaneous MVA-BN 1 x 10^8																					
Day 29	Intradermal MVA-BN 2 x 10^7																					
	Intradermal MVA-BN 1 x 10^7																					
	Subcutaneous MVA-BN 1 x 10^8																					
Max Severity Post Baseline	Intradermal MVA-BN 2 x 10^7																					
	Intradermal MVA-BN 1 x 10^7																					
	Subcutaneous MVA-BN 1 x 10^8																					

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments.
N = Number of participants in the Safety Population with non-missing data at timepoint.
n = Number of participants experiencing the given severity.

Tables with similar format:

Table 85: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Systolic Blood Pressure

Table 86: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Pulse

14.4 Summary of Concomitant Medications

Table 87: Number and Percentage of Participants with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]								
	[ATC 2 - 1]								
	[ATC 2 - 2]								
	[ATC 2 - 3]								
[ATC Level 1 – 2]	[ATC 2 - 1]								
	[ATC 2 - 2]								
	[ATC 2 - 3]								

N = Number of participants in the Safety Population.
n = Number of participants reporting taking at least one medication in the specific WHO Drug Class.

14.5 Participant Reported Tolerability

Table 88: Participant Reported Tolerability by Treatment Group

Tolerability Question	Participant Response	Intradermal MVA-BN 2 x 10^7 (N=X)		Intradermal MVA-BN 1 x 10^7 (N=X)		Subcutaneous MVA-BN 1 x 10^8 (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%
Based on your experience with the first dose of the vaccine, do you plan to receive your second dose of vaccine in the study on day 29?	Yes	x	xx	x	xx	x	xx	x	xx
	No, Any Reason								
	No, Reason A								
	No, Reason B								
	No, Other Reason								
	Missing								
Based on your experience with the study vaccine, would you be willing to take it again if recommended by your healthcare provider?	Yes								
	No, Any Reason								
	No, Reason A								
	No, Reason B								
	No, Other Reason								
	I don't know								
	Missing								
Based on your experience with the study vaccine, would you recommend it to a family member or friend if it was recommended by their healthcare provider?	Yes								
	No, Any Reason								
	No, Reason A								
	No, Reason B								
	No, Other Reason								
	I don't know								
	Missing								

N = Number of participants in the Safety Population.
n = Number of participants responding.

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

10.1 Disposition of Participants

Figure 1: CONSORT Flow Diagram

[Implementation note: The figure below is an example only. Groups presented will be Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, and Subcutaneous MVA-BN 1 x 10^8. Analysis populations presented will be safety, mITT, and PP.]

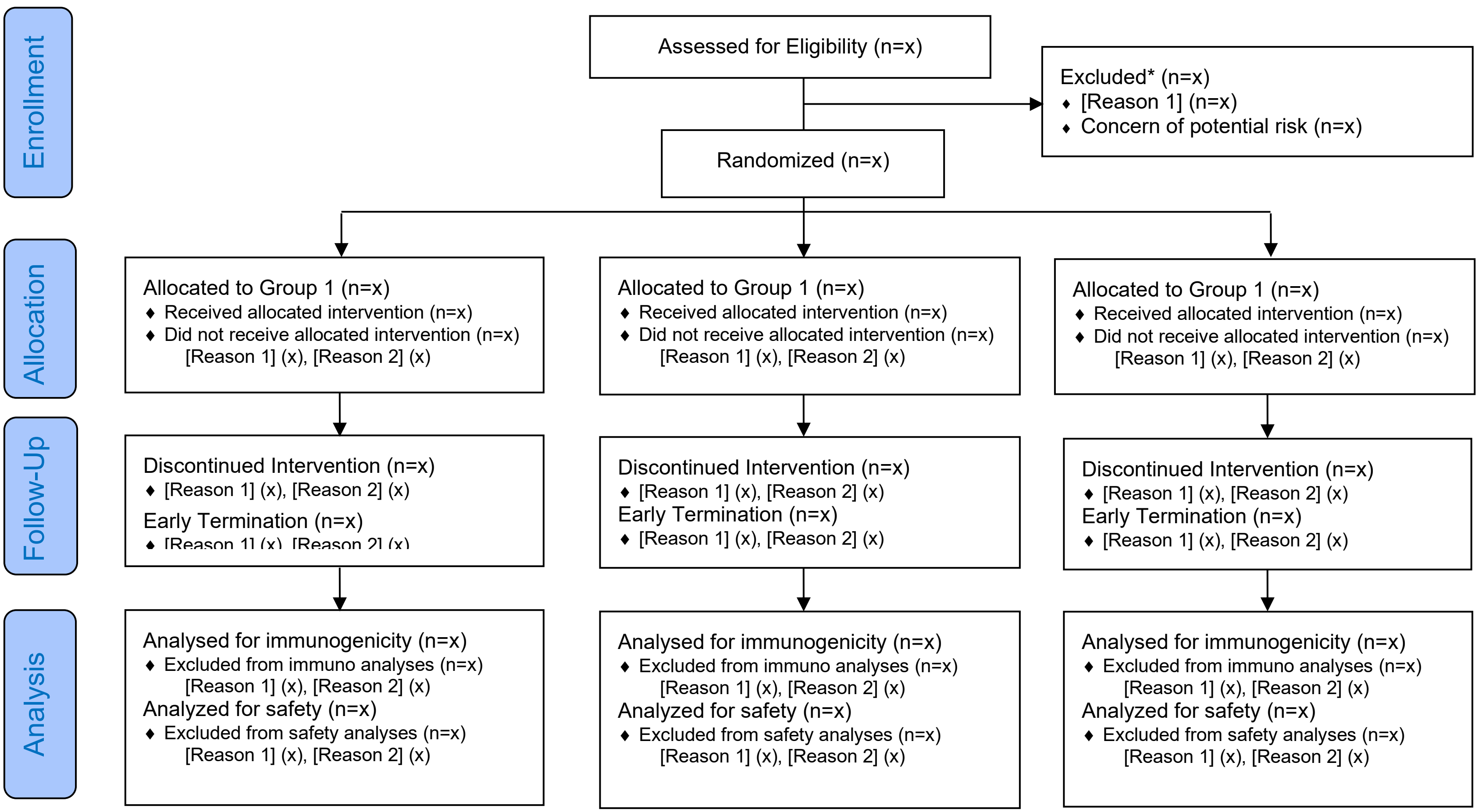
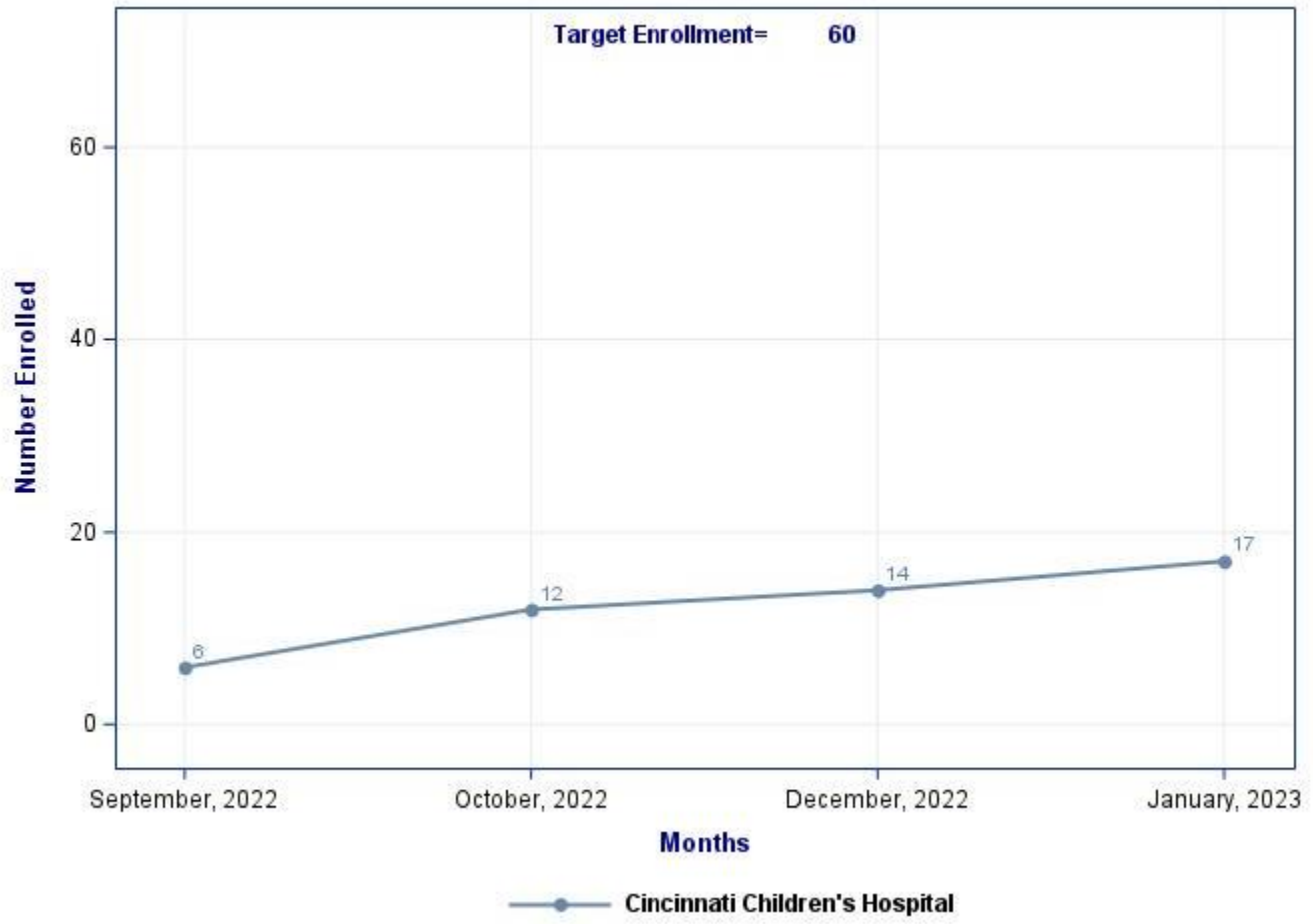


Figure 2: Enrollment Over Time

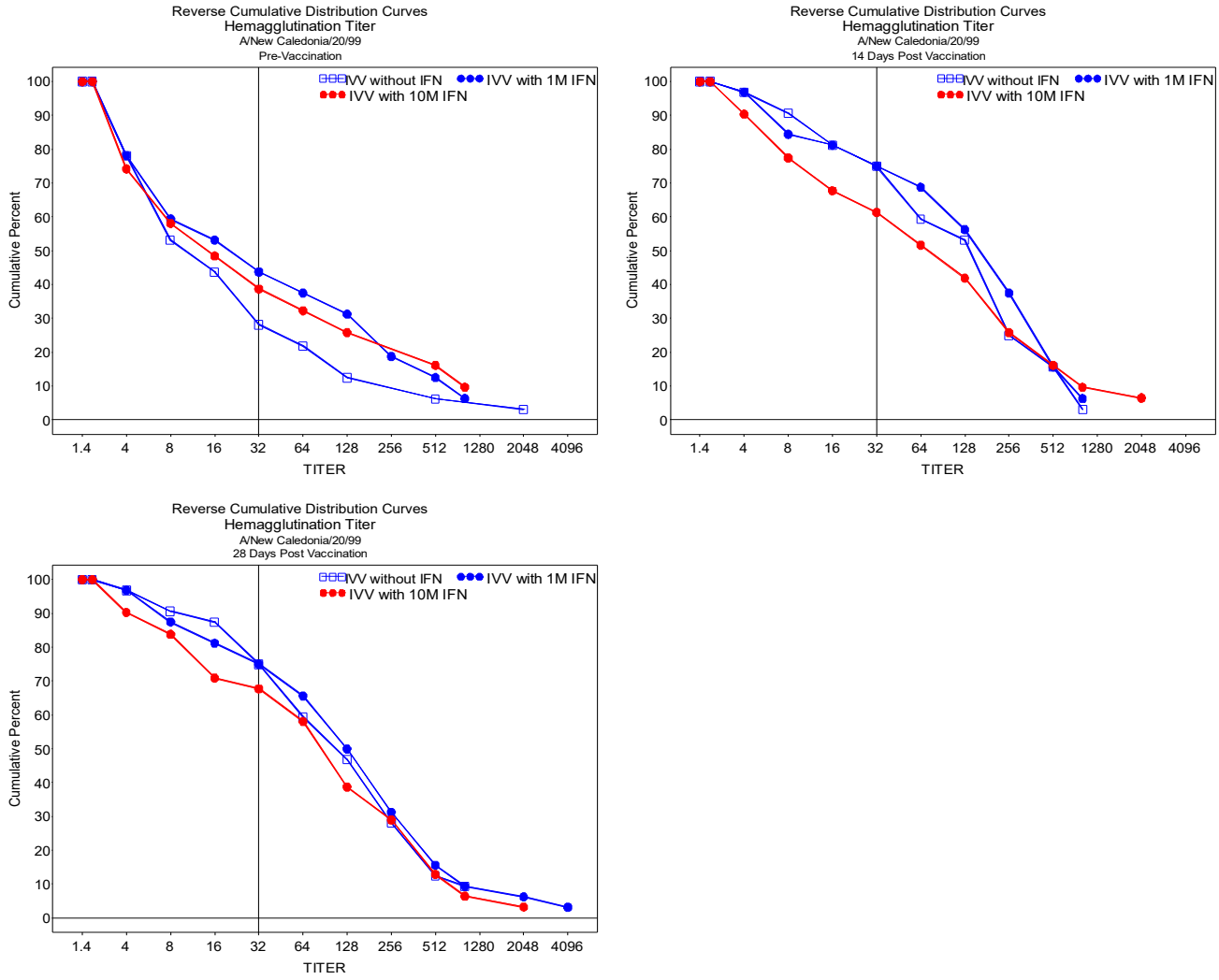
[Implementation note: The figure below is an example only. Three lines for Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, and Subcutaneous MVA-BN 1 x 10^8 enrollments and one for concurrent CDC case counts [16]will be presented.]



14.2.2 Immunogenicity Response Figures by Measure, Treatment/Vaccination, and Time Point

Figure 3: Reverse Cumulative Distribution of Vaccinia virus specific PRNT by Time Point and Treatment Group, mITT Population

[Implementation note: The figure below is an example only. Groups presented will be Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, and Subcutaneous MVA-BN 1 x 10^8 and the figure will include 8 panels for Study Day 1, 15, 29, 43, 57, 90, 181, and 365.]



Figures with similar format:

Figure 4: Reverse Cumulative Distribution of Vaccinia virus specific PRNT by Time Point and Treatment Group, Per Protocol Population

Figure 5: Reverse Cumulative Distribution of Monkeypox virus specific PRNT by Time Point and Treatment Group, mITT Population

Figure 6: Reverse Cumulative Distribution of Monkeypox virus specific PRNT by Time Point and Treatment Group, Per Protocol Population

Figure 7: Reverse Cumulative Distribution of Monkeypox virus specific PRNT by Time Point and Treatment Group, mITT Population

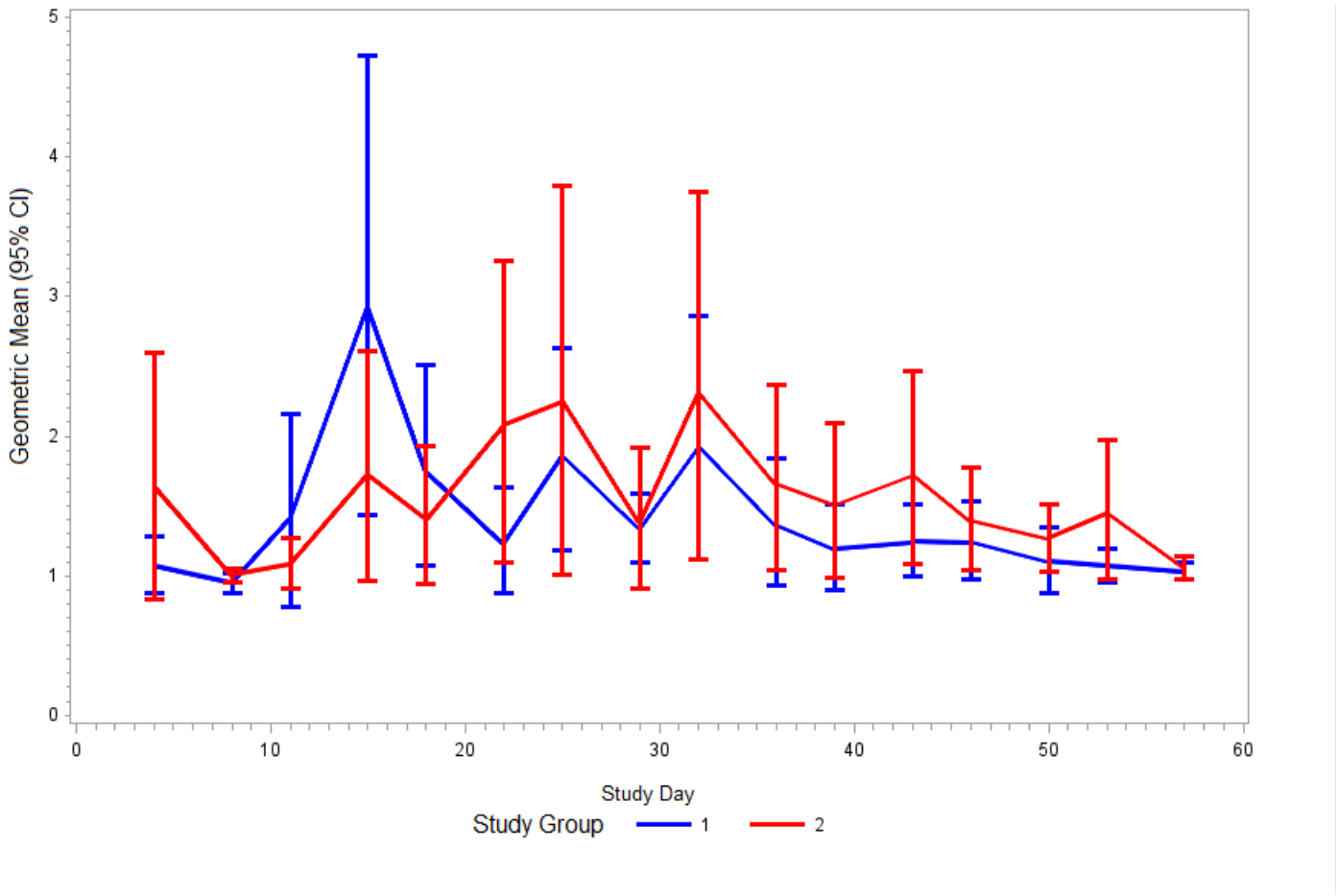
Figure 8: Reverse Cumulative Distribution of Monkeypox virus specific PRNT by Time Point and Treatment Group, Per Protocol Population

Figure 9: Reverse Cumulative Distribution of Monkeypox virus specific PRNT by Time Point and Treatment Group, mITT Population

Figure 10: Reverse Cumulative Distribution of Monkeypox virus specific PRNT by Time Point and Treatment Group, Per Protocol Population

Figure 11: GMT of Vaccinia virus specific PRNT by Time Point and Treatment Group, mITT Population

[Implementation note: The figure below is an example only. Groups presented will be Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, and Subcutaneous MVA-BN 1 x 10^8. Timepoints presented will be Study Day 1, 15, 29, 43, 57, 90, 181, and 365.]



Figures with similar format:

Figure 12: GMT of Vaccinia virus specific PRNT by Time Point and Treatment Group, Per Protocol Population

Figure 13: GMT of Monkeypox virus specific PRNT by Time Point and Treatment Group, mITT Population

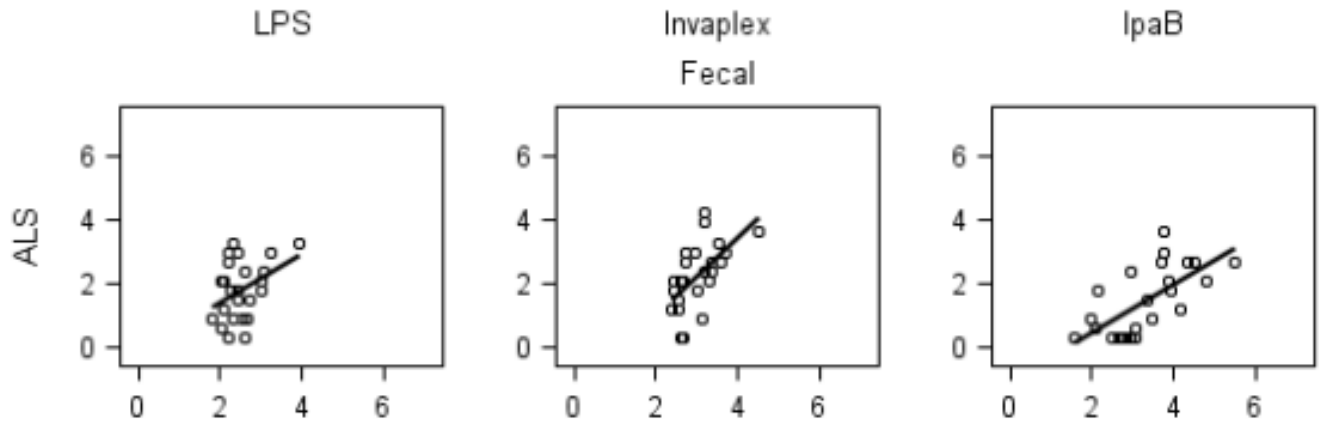
Figure 14: GMT of Monkeypox virus specific PRNT by Time Point and Treatment Group, Per Protocol Population

Figure 15: GMT of Anti-MVA Neutralizing Antibody by Time Point and Treatment Group, mITT Population

Figure 16: GMT of Anti-MVA Neutralizing Antibody by Time Point and Treatment Group, Per Protocol Population

Figure 19: Correlations by Time Point and Treatment Group, mITT Population

[Implementation note: The figure below is an example only. Timepoint presented will be Day 43. Vaccinia virus specific PRNT values will be presented on the y-axis with Monkeypox virus specific PRNT (panel 1), Anti-MVA Neutralizing Antibody (panel 2), or Anti-MPXV clade I Neutralizing Antibody (panel 3) on the x-axis.]



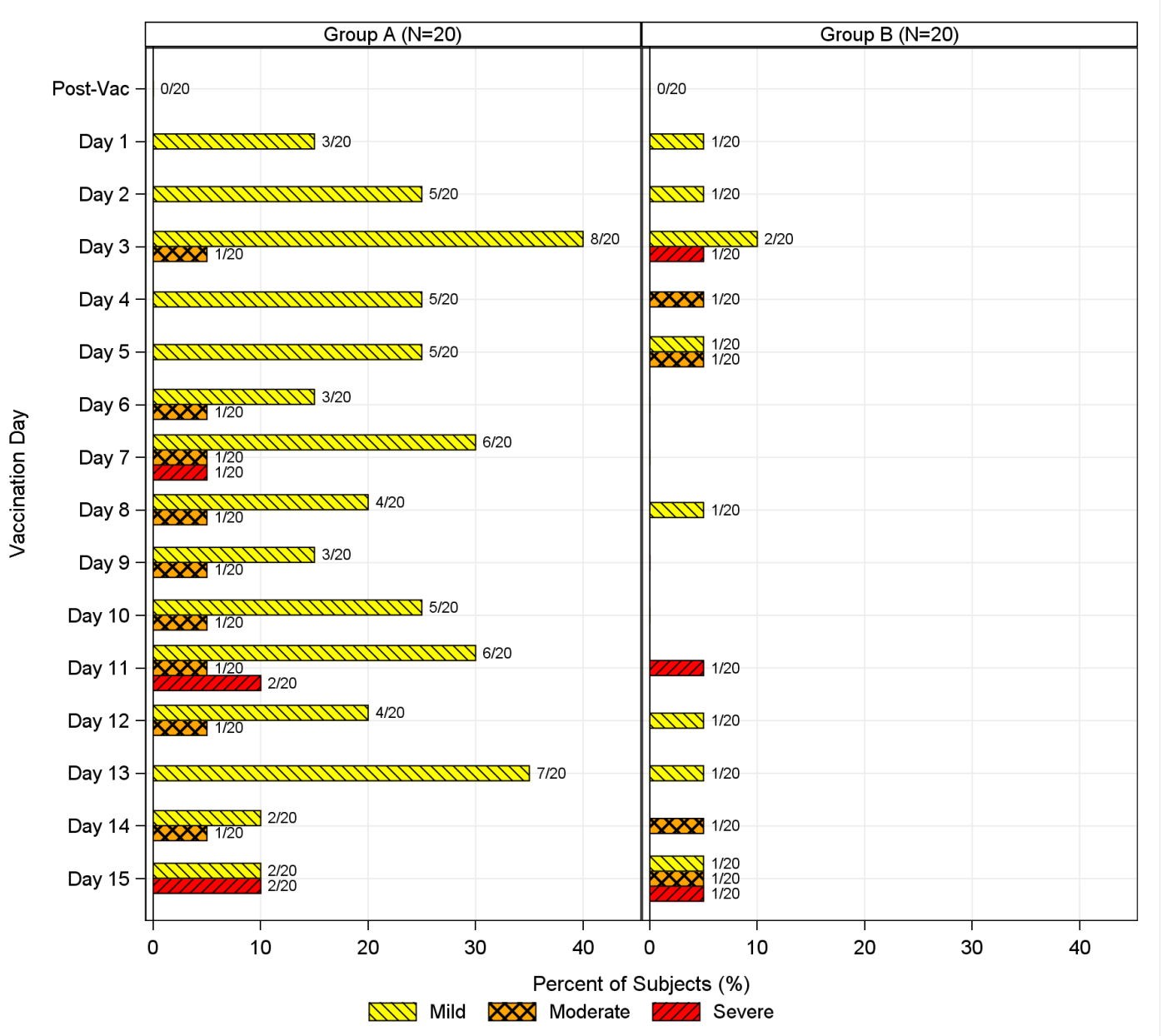
Figures with similar format:

Figure 20: Correlations by Time Point and Treatment Group, Per Protocol Population

14.3.1.1 Solicited Adverse Events

Figure 21: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Dose 1

[Implementation note: The figure below is an example only. Groups presented will be Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, and Subcutaneous MVA-BN 1 x 10^8. Severities presented will be mild (yellow with black left-diagonal strip pattern), moderate (orange with black lattice pattern), severe(red with black right-diagonal strip pattern), and life-threatening (solid black).]



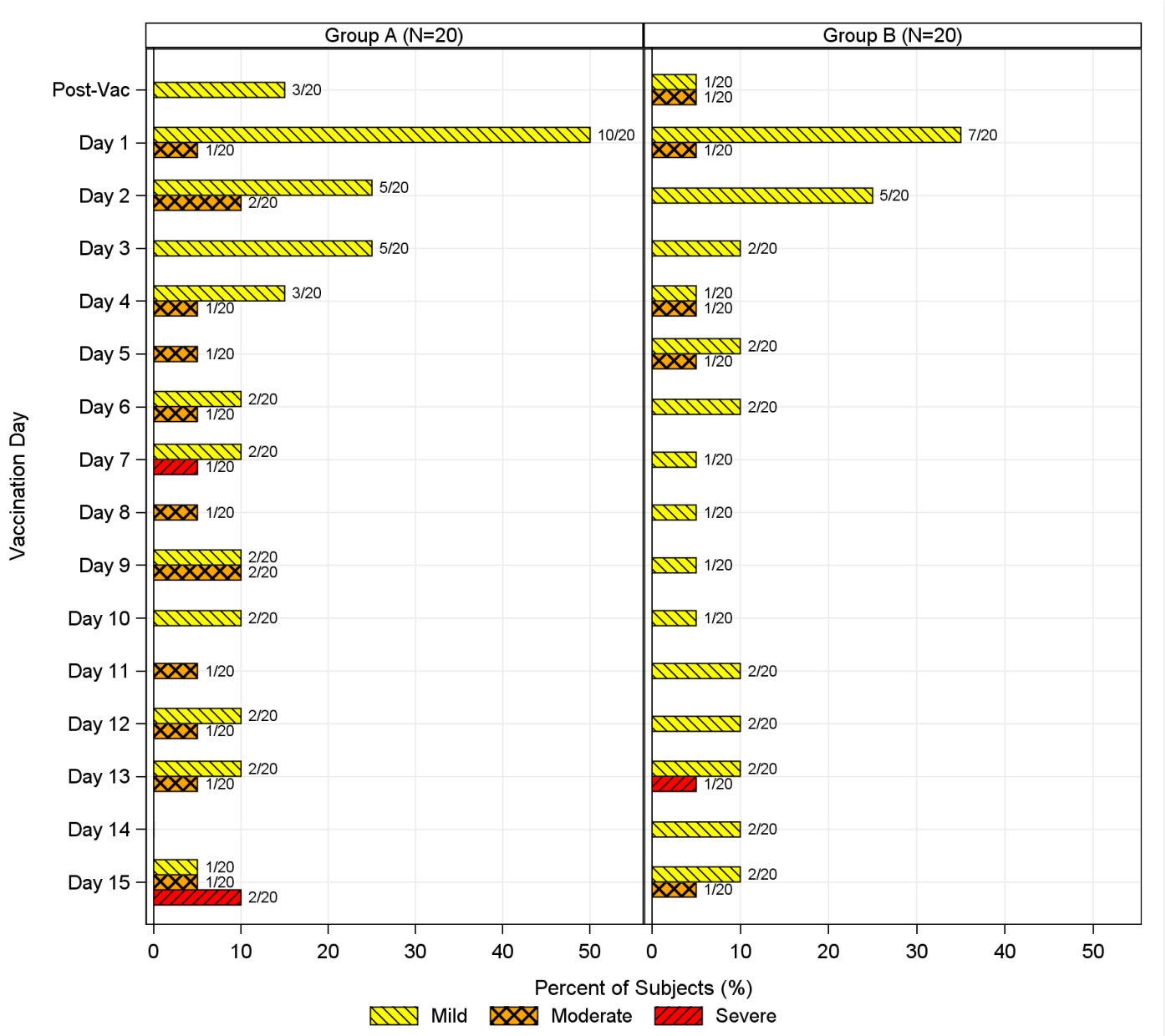
Figures with similar format:

Figure 22: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Dose 2

Figure 23: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Either Dose

Figure 24: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Dose 1

[Implementation note: The figure below is an example only. Groups presented will be Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, and Subcutaneous MVA-BN 1 x 10^8. Severities presented will be mild (yellow with black left-diagonal strip pattern), moderate (orange with black lattice pattern), severe(red with black right-diagonal strip pattern), and life-threatening (solid black).]



Figures with similar format:

Figure 25: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Dose 2

Figure 26: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Either Dose

14.3.1.2 Unsolicited Adverse Events

Figure 27: Frequency of Related Adverse Events by MedDRA System Organ Class and Severity

[Implementation note: The figure below is an example only. Groups presented will be Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, and Subcutaneous MVA-BN 1 x 10^8. Severities presented will be mild (yellow with black left-diagonal strip pattern), moderate (orange with black lattice pattern), severe(red with black right-diagonal strip pattern), and life-threatening (solid black).]

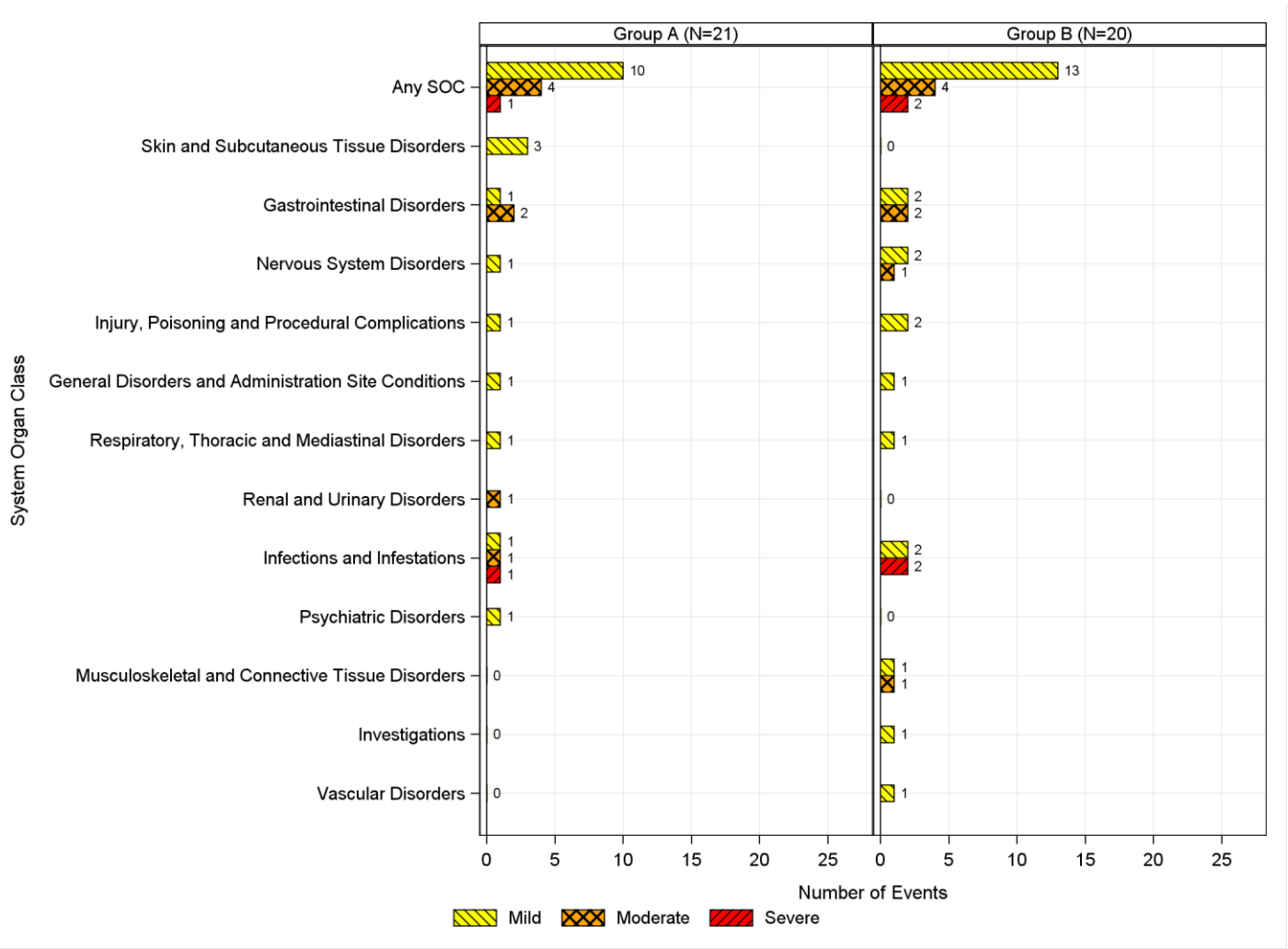
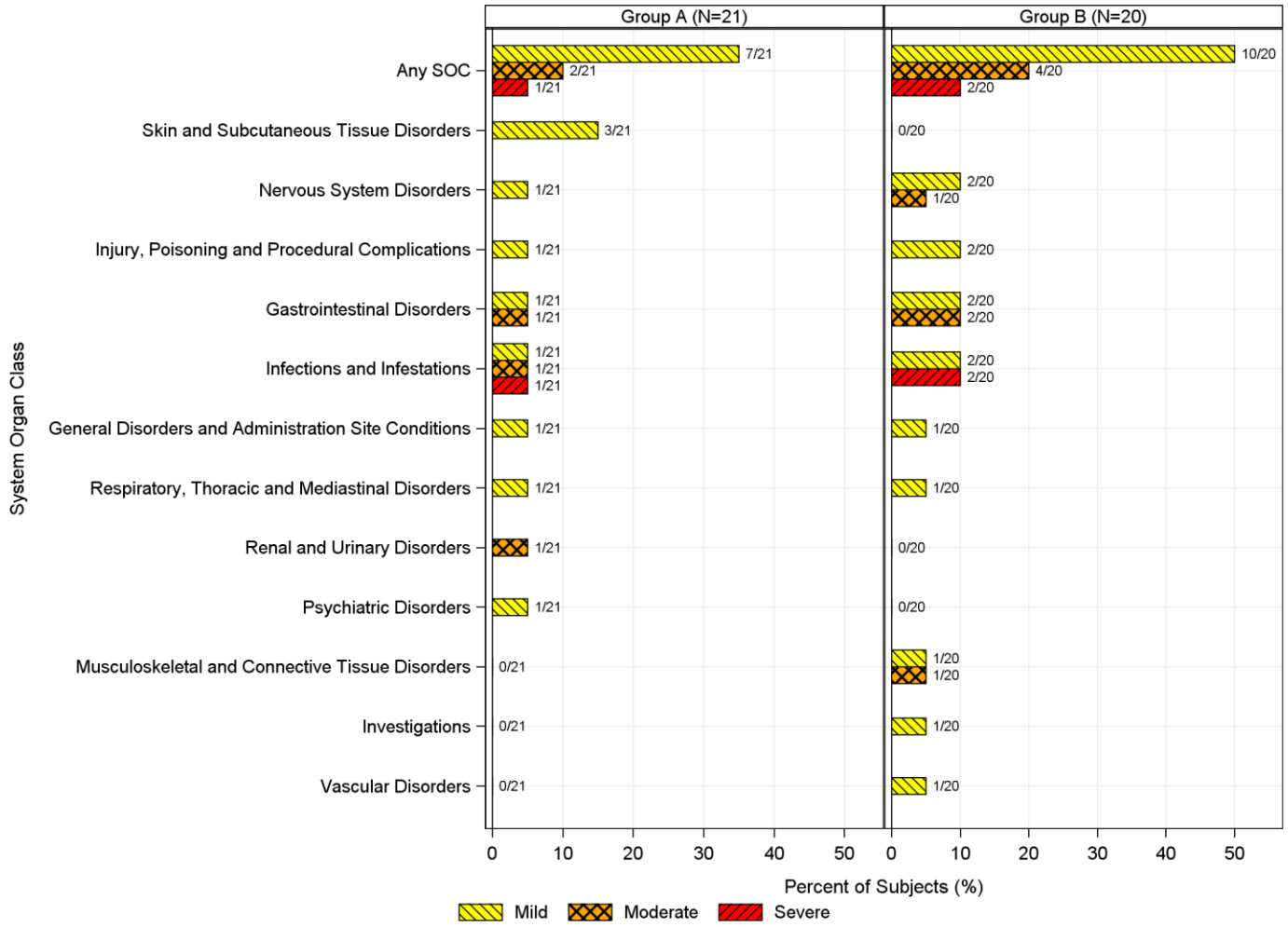


Figure 28: Incidence of Related Adverse Events by MedDRA® System Organ Class and Maximum Severity

[Implementation note: The figure below is an example only. Groups presented will be Intradermal MVA-BN 2 x 10^7, Intradermal MVA-BN 1 x 10^7, and Subcutaneous MVA-BN 1 x 10^8. Severities presented will be mild (yellow with black left-diagonal strip pattern), moderate (orange with black lattice pattern), severe(red with black right-diagonal strip pattern), and life-threatening (solid black).]



APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

Listing 1: **Listing of Participants Receiving Investigational Product**

(not included in SAP, but this is a placeholder for the CSR)

16.2 Database Listings by Participant

16.2.1 Discontinued Participants

Listing 2: Early Terminations or Discontinued Participants

Treatment Group	Participant ID	Category	Reason for Early Termination or Treatment Discontinuation	Study Day

16.2.2 Protocol Deviations

Listing 3: Participant-Specific Protocol Deviations

Treatment Group	Participant ID	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	UP?	Deviation Resolution	Comments

Listing 4: Non-Participant-Specific Protocol Deviations

Site	Start Date	Deviation	End Date	Reason for Deviation	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	UP?	Deviation Category	Deviation Resolution	Comments

16.2.3 Participants Excluded from Analysis

Listing 5: Participants Excluded from Analysis Populations

Treatment Group	Participant ID	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant Excluded
		[e.g., Safety, mITT, PP]	[e.g., Safety, mITT, PP, Day x]		
Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.					

16.2.4 Demographic Data

Listing 6: Demographic Data

Treatment Group	Participant ID	Sex at Birth	Gender Identity	Sexual Identity	Age at Enrollment (years)	Ethnicity	Race	HIV Status

Listing 7: Pre-Existing and Concurrent Medical Conditions

Treatment Group	Participant ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

16.2.5 Compliance and/or Drug Concentration Data (if available)

Not applicable.

16.2.6 Individual Immunogenicity Response Data

Listing 8: Individual Immunogenicity Response Data

Treatment Group	Participant ID	HIV Status	Planned Time Point	Actual Study Day	Assay	Titer

16.2.7 Adverse Events

Listing 9: Solicited Events – Systemic Symptoms

Treatment Group	Participant ID	Dose Number	Post Dose Day	Assessment[a]	Symptom	Severity	Attributed to Alternate Etiology?[b]	Alternate Etiology
				MA				
				Clinic				

[a] MA = Data reported by participant on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.
[b] Grade 3 and Grade 4 events only.
Note: Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

Listing 10: Solicited Events – Local Symptoms

Treatment Group	Participant ID	Dose Number	Post Dose Day	Assessment[a]	Symptom	Severity
				MA		
				Clinic		

[a] MA = Data reported by participant on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.
Note: Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

Listing 11: Unsolicited Adverse Events

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	Severity	SAE?	SUSAR?	MAAE?	UP?	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Treatment Group: , Participant ID: , AE Number:														
Comments:														
Treatment Group: , Participant ID: , AE Number:														
Comments:														
Note: For additional details about SAEs, see Table 78.														

Listing 12: Illness Visits

Treatment Group	Participant ID	Study Day of Illness Onset	Study Day of Illness Visit	Positive Test for Mpox Infection form Outside Lab	Study Day of Test
				Yes or No	

16.2.8 Individual Laboratory Measurements

Not applicable.

16.2.9 Vital Signs and Physical Exam Findings

Listing 13: Vital Signs

Treatment Group	Participant ID	Planned Time Point	Actual Study Day	Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (beats/min)

Listing 14: Physical Exam Findings

Treatment Group	Participant ID	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)

16.2.10 Concomitant Medications

Listing 15: Concomitant Medications

Treatment Group	Participant ID	Concomitant Medications Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)

16.2.11 Pregnancy Reports

Listing 16: Pregnancy Reports – Maternal Information

Treatment Group	Participant ID	Pregnancy Number	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?
Note: Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.											

Listing 17: Pregnancy Reports – Gravida and Para

			Live Births												
Participant ID	Pregnancy Number	Gravida	Extremely PB[a]	Very Early PB[a]	Early PB[a]	Late PB[a]	Early TB[b]	Full TB[b]	Late TB[b]	Post TB[b]	Still Births	Spontaneous Abortion/ Miscarriage	Elective Abortions	Therapeutic Abortions	Major Congenital Anomaly with Previous Pregnancy?
Note: Gravida includes the current pregnancy, para events do not.															

[a] Preterm Birth
[b] Term Birth

Listing 18: Pregnancy Reports – Live Birth Outcomes

Participant ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score, 1 minute	Apgar Score, 5 minutes	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?
Note: Congenital Anomalies are included in the Adverse Event listing.												

Listing 19: Pregnancy Reports – Still Birth Outcomes

Participant ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?

Listing 20: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Participant ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion

Listing 21: Participant Reported Tolerability

Treatment Group	Participant ID	Tolerability Question	Response	Sponsor Determined Reason Category	Verbatim Reason