ADDENDUM

Center for Biologics Evaluation and Research
Office of Biostatistics and Pharmacovigilance

CBER Surveillance Program

Safety Surveillance of Vaccines Used for Mpox Prevention: Protocol Addendum

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Study Team

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VERSION CONTROL

Version	Description	Date
v1.0	Protocol to describe methods for descriptive safety monitoring of vaccines used to prevent mpox	12/16/2022
Addendum	Addendum to describe methods of the medical record review process	6/19/2023

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This document is intended to serve as an addendum to the Safety Surveillance of Vaccines Used for Mpox Prevention: Active Monitoring Master Protocol. The background, overview, data sources, and quality assurance are described in depth in the master protocol and are not covered here. This addendum will describe the objective and methodology for summarizing mpox diagnoses in administrative commercial insurance claims databases and the associated medical record review activities.

1. Objectives

The primary objective of this protocol addendum is to describe the characteristics of the population diagnosed with mpox using commercial claims and medical record data.

2. Mpox Diagnosis Descriptive Analysis in Administrative Claims Data

2.1 Study Population

The study population will be people 18–64 years of age who are enrolled in a commercial health insurance plan covered in one of the three claims databases previously described (i.e., CVS Health Clinical Trial, Optum, and Carelon Research (formerly HealthCore, Inc.)) and who had a mpox diagnosis during the study period. Participants will enter the study cohort on the first day of the study period. Participants are required to have date of birth and continuous enrollment prior to the incident mpox diagnosis. If the mpox diagnosis occurs on or before May 1, 2023, continuous enrollment from May 1, 2022 is required. If the mpox diagnosis occurs after May 1, 2023, at least 365 days of continuous enrollment is required.

2.2 Study Period

The study period will be the same as in the safety surveillance analysis (i.e., May 10, 2022 until no longer deemed necessary by the United States Food and Drug Administration (FDA)).

2.3 Event Definitions

Mpox diagnoses will be identified by the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10 CM) diagnosis code "B04" in administrative claims from the facility inpatient, facility outpatient emergency department, other facility outpatient, or professional services (as defined in the analysis code list). To avoid repeated counts for the same infection, the first incident medically attended mpox diagnosis in the study period will be uniquely counted per person, where an incident mpox diagnosis is defined as a diagnosis without another prior mpox diagnosis since May 1, 2022 (if the diagnosis is on or before May 1, 2023) or in the 365 days prior (if the diagnosis is after May 1, 2023).

Vaccine exposure will be identified as in the master protocol (i.e., using product codes occurring in any care setting). If a person receives multiple vaccine brands they will be excluded from the medical record review. ACAM2000 and JYNNEOS vaccination history will be determined from May 10, 2022.

2.4 Descriptive Analyses

We will use descriptive statistics to summarize the characteristics of people diagnosed with mpox in administrative claims data who had 1) no prior history of vaccination with ACAM2000 or JYNNEOS before diagnosis and 2) those with an mpox diagnosis occurring $\geq$ 14 days after receipt of at least one JYNNEOS dose. Data will be stratified by sex, age, and age and sex. Descriptive statistics will be updated monthly until no longer deemed necessary by FDA. An example table representing the proposed descriptive statistics can be found below in **Table 1**.

Table 1. Characteristics of people with mpox diagnoses in administrative claims data in relationship to a JYNNEOS Vaccination

Characteristic		Mpox Diagnosis							
		Overall		No history of vaccination		≥14 days after JYNNEOS Dose 1		≥14 days after JYNNEOS Dose 2	
		#	%	#	%	#	%	#	%
Total									
Sex									
Female									
Male									
Age									
18-25									
…									
56-64									
Age*Sex									
18-25									
…									
56-64									

Note: Separate tables will be provided for each Data Partner.

3. Mpox Diagnosis Descriptive Analysis in Medical Record Data

3.1 Objectives

We will use medical record data to summarize demographic and clinical characteristics of patients who had a mpox diagnosis with 1) no prior history of vaccination with ACAM2000 or JYNNEOS before mpox diagnosis (group one) and 2) those with an mpox diagnosis occurring ≥14 days after receipt of at least one JYNNEOS dose (group two).

3.2 Selection and Specifications

Medical records will be sampled and requested based on administrative insurance claims and Immunization Information System (IIS) data for both groups. For group one, a random sample of records will be requested for patients who had an incident mpox diagnosis (as defined in Section 2.3) *and* had no prior history of ACAM2000 or JYNNEOS vaccination before the diagnosis recorded in claims data. Records will be sampled from each data partner in order to receive a cumulative total of 50-100 records across all sources.

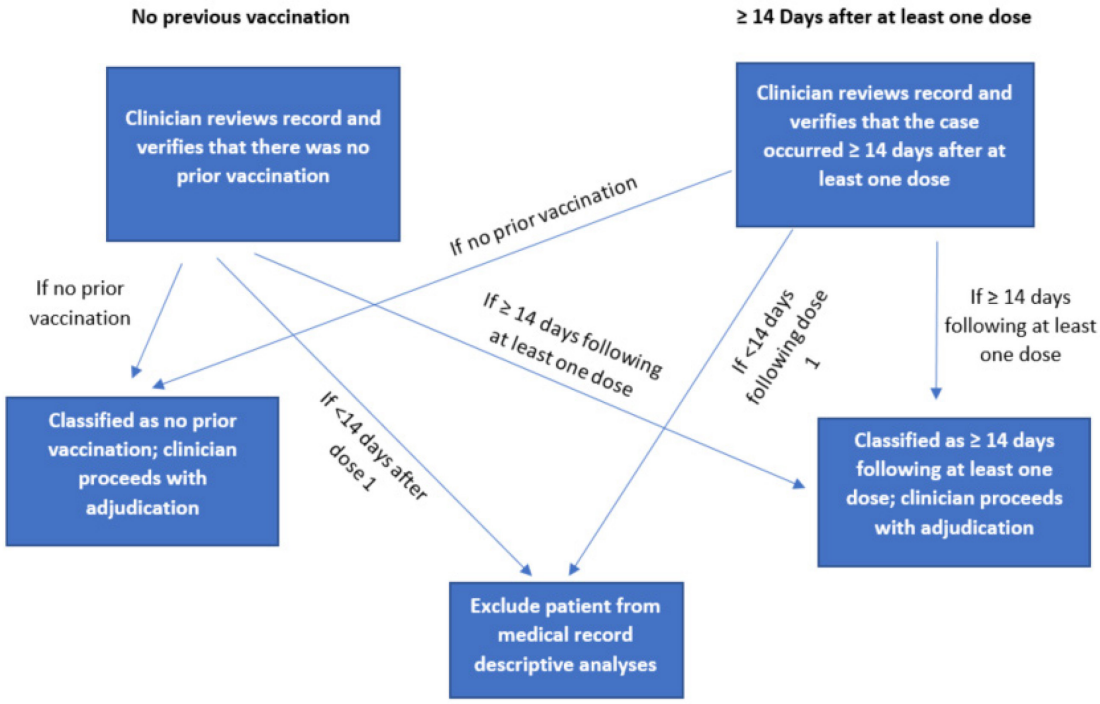
For group two, all records for patients with an incident mpox diagnosis (as defined in Section 2.3) occurring ≥14 days following a second JYNNEOS dose will be requested. The remainder of the cases following just one JYNNEOS dose will be sampled so that we receive a cumulative total of 50-100 group two records across all sources. These will be one-time record requests. Records will be sampled for each data partner separately.

Specifications will be anchored on the relevant diagnosis date. There will be a window of 3 days prior to and 30 days after the diagnosis date to identify relevant providers. All records from relevant providers will be requested from 3 days prior to 90 days following diagnosis date. The timeframe will be truncated at the time of the request for those who were not outside of the 90-day period at the time of the request.

3.3 Event Definitions

For group one, data from medical records will be reviewed to verify the person experienced an incident mpox diagnosis and had no prior history of ACAM2000 or JYNNEOS vaccination before diagnosis. For group two, data from medical records will be used to verify that the person experienced an incident mpox diagnosis occurring ≥14 days after receipt of at least one JYNNEOS dose. **Figure 1** describes the process for classifying received medical records into Group 1 or Group 2. Group 2 will be further split into sections: after dose 1, and after dose 2; which will be reviewed following the same structure outlined in the figure below.

Figure 1. Categorization of received medical records



3.4 Clinical Adjudicators

An infectious disease specialist and general medicine practitioners will perform adjudication and abstraction of medical records using a standardized case report form. The CDC case definition for use in the 2022 mpox response will be used to perform this review.

3.5 Data Analysis

Demographic and clinical data which is abstracted from medical records will be summarized using descriptive statistics.