Vaccines and Related Biological Products Advisory Committee October 22, 2020 Meeting Presentation

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CBER Plans for Monitoring COVID-19 Vaccine Safety and Effectiveness

Steve Anderson, PhD, MPP
Director, Office of Biostatistics & Epidemiology, CBER

VRBPAC Meeting
October 22, 2020

FDA Vaccine Surveillance: Pre-licensure Pharmacovigilance Planning

"Safety throughout the lifecycle" approach for vaccines (pre- and post-licensure):

- Manufacturer submits pharmacovigilance plans (PVP) of proposed post-licensure surveillance activities
  - Submitted for BLA and for EUA
  - Post-licensure commitment (PMC) – studies, registries for general safety concern
  - Post-licensure requirement (PMR) – clinical study, epidemiological study, registries, etc. to verify a specific safety signal
  - Routine pharmacovigilance – Passive surveillance (VAERS), review of safety literature, available studies, etc.

FDA Vaccine Surveillance Programs: Post-Licensure

1. **Passive Surveillance of Vaccines**
   - Vaccine Adverse Event Reporting System (VAERS)
     - Management shared by CDC and FDA

2. **Active Surveillance Monitoring Program**
   - FDA BEST
   - FDA-CMS partnership

FDA Vaccine Surveillance Programs: Post-Licensure

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VAERS

Vaccine Adverse Event Reporting System

Co-managed by CDC and FDA

CDC + FDA

http://vaers.hhs.gov

VAERS – FDA CBER Efforts

- CDC presentation covered VAERS so will provide summary of FDA efforts
- **FDA and CDC have weekly and bi-weekly coordination meetings** on VAERS and Pharmacovigilance activities between CBER OBE and OBE Division of Epidemiology (DE) and CDC Immunization Safety Office
- **CBER DE Physicians will be reviewing the serious adverse event reports** from VAERS for COVID-19 vaccines – review of individual reports, death reports, conduct aggregate analyses, case-series, etc.
- **FDA will utilize statistical data-mining methods** to detect disproportional reporting of specific vaccine-adverse event combinations to identify AEs that are more frequently reported

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FDA Vaccine– Legislative Authorization Active Surveillance

Legislation, mandates and Current Surveillance

FDA Amendments Act of 2007:

- Directed FDA to develop an active risk identification and analysis system – such as Sentinel, and later BEST, and others and covers ≥100 million persons

Prescription Drug User Fee Act VI (2017)

- Discussion between FDA and Industry on Priority Areas - Renewed every 5 yrs
- Provides resources/funding for Sentinel, BEST, real-world evidence, etc

COVID-19 Vaccine Monitoring Data Considerations

- **Rapid data access** for near real time surveillance
- **Large databases of tens of millions of patients** for evaluating vaccine rare serious adverse events
- **Data representing integrated care spectrum** – outpatient, physician, inpatient, etc.
- **High quality data** to assess and confirm potential adverse events or safety concerns for COVID-19 vaccines
- **Data with significant clinical detail** or medical chart access

1. FDA Biologics Effectiveness and Safety (BEST) System

- Several partners – Acumen, IBM Watson, IQVIA, OHDSI, HealthCore, Humana, Optum, Healthagen, Academic organizations
- Represents variety of healthcare settings – inpatient, emergency department, outpatient, etc.

BEST Initiative Expansion

CLAIMS Data Sources

Data Sources	Type	Patients (millions)
MarketScan	Claims	254
Blue Health Intelligence	Claims	33.6
Optum	Claims	70
HealthCore	Claims	56
Healthagen	Claims	26
OneFlorida Clinical Research Consortium (Medicaid)	Claims	6.7

Data lag: 1-12 months depending on data source

BEST Initiative Expansion
EHR Data Sources

Data Sources	Type	Patients (millions)
MedStar Health	EHR	6
IBM Explorys	EHR	90
Regenstrief Institute	Claims and EHR	20.2
Columbia University	EHR	6.6
University of Colorado	EHR	17
University of California San Francisco	EHR	3.2
PEDSnet Clinical Research Consortium	EHR	6.2
Optum EHR	EHR	105
OneFlorida Clinical Research Consortium	EHR	5.6
OneFlorida Clinical Research Consortium	Linked EHR-Claims	1.5
MarketScan Explorys Claims-EHR (CED)	Linked EHR-Claims	5.5
Optum	Linked EHR-Claims	50

Data lag: 1-2 weeks to 4 months depending on data source

2. CMS (Center for Medicare & Medicaid Services)

- **Federal Partners**
  - Ongoing FDA-CMS partnership on vaccine safety since 2002
  - Data cover very large population of approximately 55 million elderly US beneficiaries ≥65yrs of age
  - >92% of US elderly use Medicare so database represents the elderly population and not a sample
  - Represents variety of healthcare settings – inpatient, outpatient, etc.
  - Consists of claims data with access to medical charts

Limitations of Data Systems

- Not all claims and EHR data systems can be used to address a vaccine safety or effectiveness regulatory question

- Each data system has its limitations
  - Populations, healthcare settings, clinical detail, necessary parameters, data lag, exposures and outcomes that are captured

FDA COVID-19 vaccine safety surveillance planning

“Near real-time surveillance” or rapid-cycle analyses (RCA)

- FDA plans on monitoring 10 -20 safety outcomes of interest to be determined based on:
  - Pre-market review of sponsor safety data submitted to FDA
  - In coordination with federal partners, international regulatory partners and organizations, academic experts, others
  - Literature and regulatory experience with similar vaccines, novel vaccine platforms, and using other relevant data
  - FDA plans on using CMS data for COVID-19 vaccine RCA – near real time with efforts

FDA Safety Surveillance of COVID-19 Vaccines :
DRAFT Working list of possible adverse event outcomes
Subject to change

- Guillain-Barré syndrome
- Acute disseminated encephalomyelitis
- Transverse myelitis
- Encephalitis/myelitis/encephalomyelitis/ meningoencephalitis/meningitis/ encepholapathy
- Convulsions/seizures
- Stroke
- Narcolepsy and cataplexy
- Anaphylaxis
- Acute myocardial infarction
- Myocarditis/pericarditis
- Autoimmune disease
- Deaths
- Pregnancy and birth outcomes
- Other acute demyelinating diseases
- Non-anaphylactic allergic reactions
- Thrombocytopenia
- Disseminated intravascular coagulation
- Venous thromboembolism
- Arthritis and arthralgia/joint pain
- Kawasaki disease
- Multisystem Inflammatory Syndrome in Children
- Vaccine enhanced disease

FDA Experience with Near Real Time Surveillance / RCA

FDA and CMS - RCA

- Conduct "near real-time" surveillance for annual influenza vaccine and Guillain-Barre Syndrome(GBS) since 2007
- Support confirmation of CDC rapid-cycle analyses of safety for seasonal influenza vaccine, Shingrix, and others

FDA Sentinel – Rapid Surveillance

- Near real-time, rapid surveillance in 2017-2018 seasonal influenza vaccine – evaluation of 6 health outcomes of interest

FDA COVID-19 vaccine safety surveillance Plans

- **Epidemiological analyses**
  - Need capability to resolve potential safety signals identified from near real-time surveillance, TreeScan and other sources
  - Rapid queries and small epidemiological studies
  - Larger self-controlled, cohort, comprehensive protocol-based studies

COVID-19 Vaccine Effectiveness Surveillance Plans

- COVID-19 vaccine(s) – there may be limited information available at licensure on level and duration of effectiveness
- Manufacturers may conduct certain COVID-19 vaccine effectiveness post-licensure studies
- FDA may conduct COVID-19 vaccine effectiveness studies
  - General effectiveness studies – including subpopulations of interest
  - Duration of protection studies
  - Others
- FDA coordinating COVID-19 Vaccine Effectiveness efforts with the CDC NCIRD through monthly, bi-monthly meetings

FDA-CMS-CDC Vaccine Effectiveness Experience

- Extensive experience with the data and methods needed to conduct vaccine effectiveness studies
- Produced several vaccine effectiveness and relative vaccine effectiveness studies for influenza and zoster vaccines
- Conducted duration of effectiveness analysis of Zostavax vaccine

FDA-CMS Vaccine Effectiveness Experience

- Actively studying risk factors for COVID-19 and preparing to study safety and effectiveness of vaccines and biologics therapies
- More than 30 publications since 2012
- Results included in Congressional testimony

CBER COVID-19 Vaccine Monitoring Transparency Considerations

- Master Protocols for Safety and Effectiveness outcomes
- Posting of draft protocols for public comment
- Posting of final protocols and final study reports on the BESTinitiative.org website

US Government-wide Efforts
COVID-19 Vaccine Monitoring

Large US Government Effort

FDA Coordinating its COVID-19 vaccine safety and effectiveness monitoring efforts with other government agencies:

- Centers for Disease Control (CDC)
- Centers for Medicare& Medicaid Services (CMS)
- Veterans Administration (VA)
- National Institutes of Health
- Department of Defense
- Indian Health Services

US Government-wide Efforts
COVID-19 Vaccine Monitoring (2)

Large US Government Effort

- Weekly meetings between FDA and CDC, regular meetings with VA and CMS
- Planned sharing of protocols, discussion safety and effectiveness outcomes of interest
- Coordinated planning and conduct of surveillance activities such as near real time surveillance/ RCA between FDA, CDC, CMS, VA, and DOD

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- CBER OBE Colleagues
- CDC Colleagues
- CMS Colleagues
- VA Colleagues
- FDA Partners: Acumen, IBM Watson – and new partners in FY2021

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Thank you!

Questions?