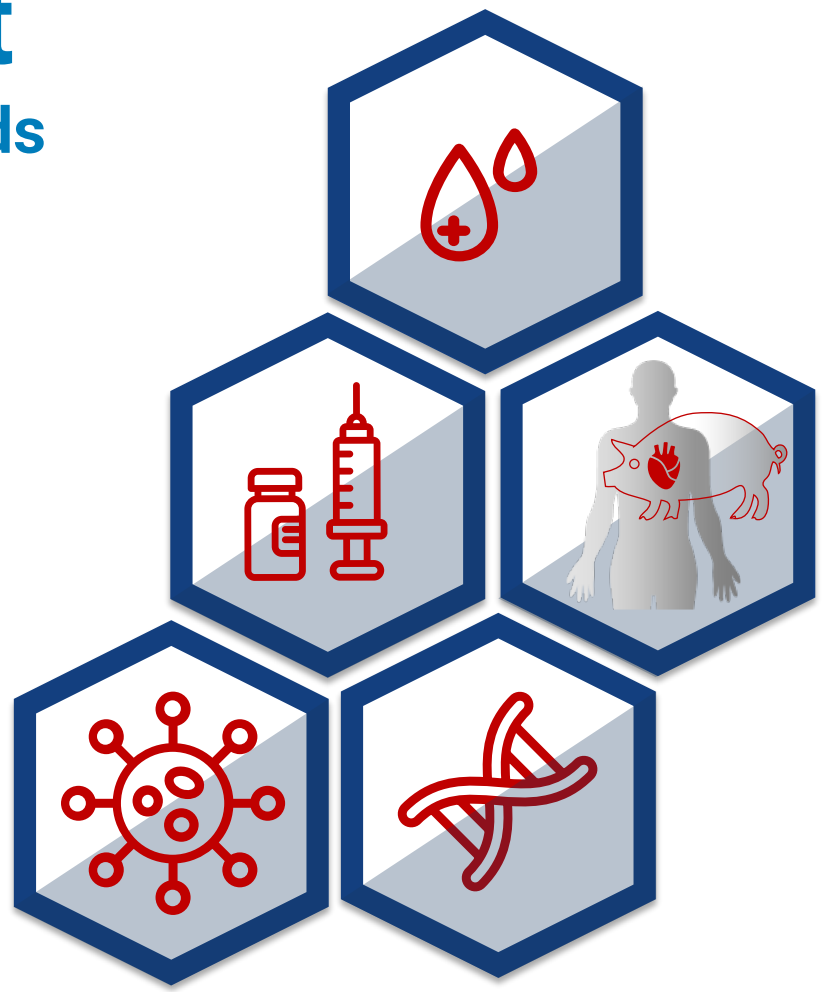
U.S. FOOD & DRUG ADMINISTRATION

CBER BEST IM Exchange Pilot

Biologics Effectiveness and Safety Innovative Methods



Hussein Ezzeldin, PhD
Analytics and Real-World Evidence Branch (ARWEB)
Division of Analytics and Benefit-Risk Assessment (DABRA)
Office of Biostatistics and Pharmacovigilance (OBPV)
Center for Biologics Evaluation and Research (CBER)

Disclaimer

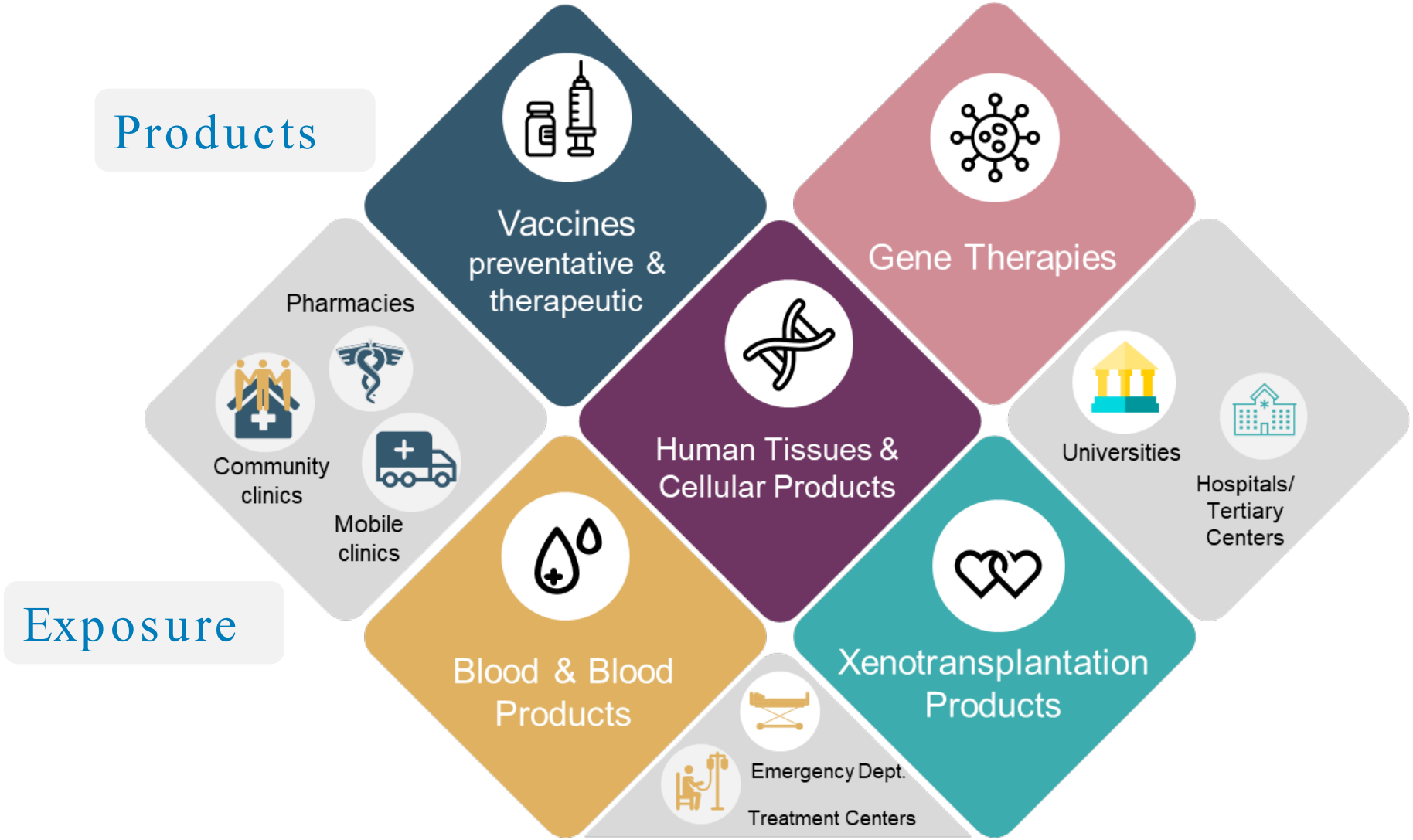
This presentation reflects the views of the presenter and should not be construed to represent FDA's views or policies.

Outline

- Background
- Exchange Pilot
- Results
- Conclusion and Summary

Background: *CBER Portfolio*

CBER-Regulated Products



Background: *Challenges*

Clinical **exposure** and potential **outcome**

Current

Manual Detection

- Individual flagging of potential AEs
- Under-recognition of outcomes

Manual Validation

- Time-intensive to review dispersed data
- Potential AEs not always communicated
- Case definitions separate

Manual Reporting

- Data re-entry to report externally
- Lack of granularity in report evidence

vs.

Future

Automated Detection

- Batch detection, more focus on patient care
- AI algorithm scores potential cases

Semi-Automated Validation

- Evidence integration reduces burden
- Flagged and prioritized cases sent for review
- Case definition integrated

Semi-Automated Reporting

- Auto-population of granular ICSR evidence
- Generation of evidence-based ICSR narrative

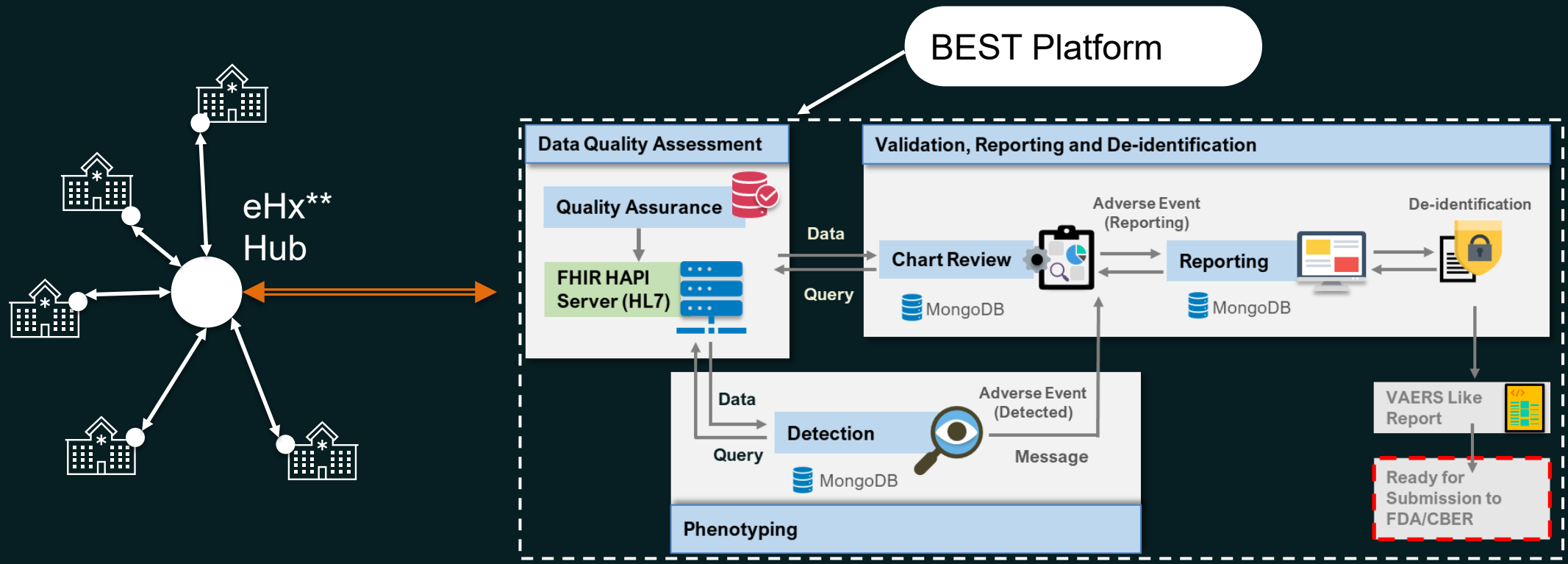
Existing Manual Process Creates Burden

BEST Platform demonstrates use of innovative methods to reduce burden, while increasing quantity and quality of AE reports

ICSR, individual case safety report

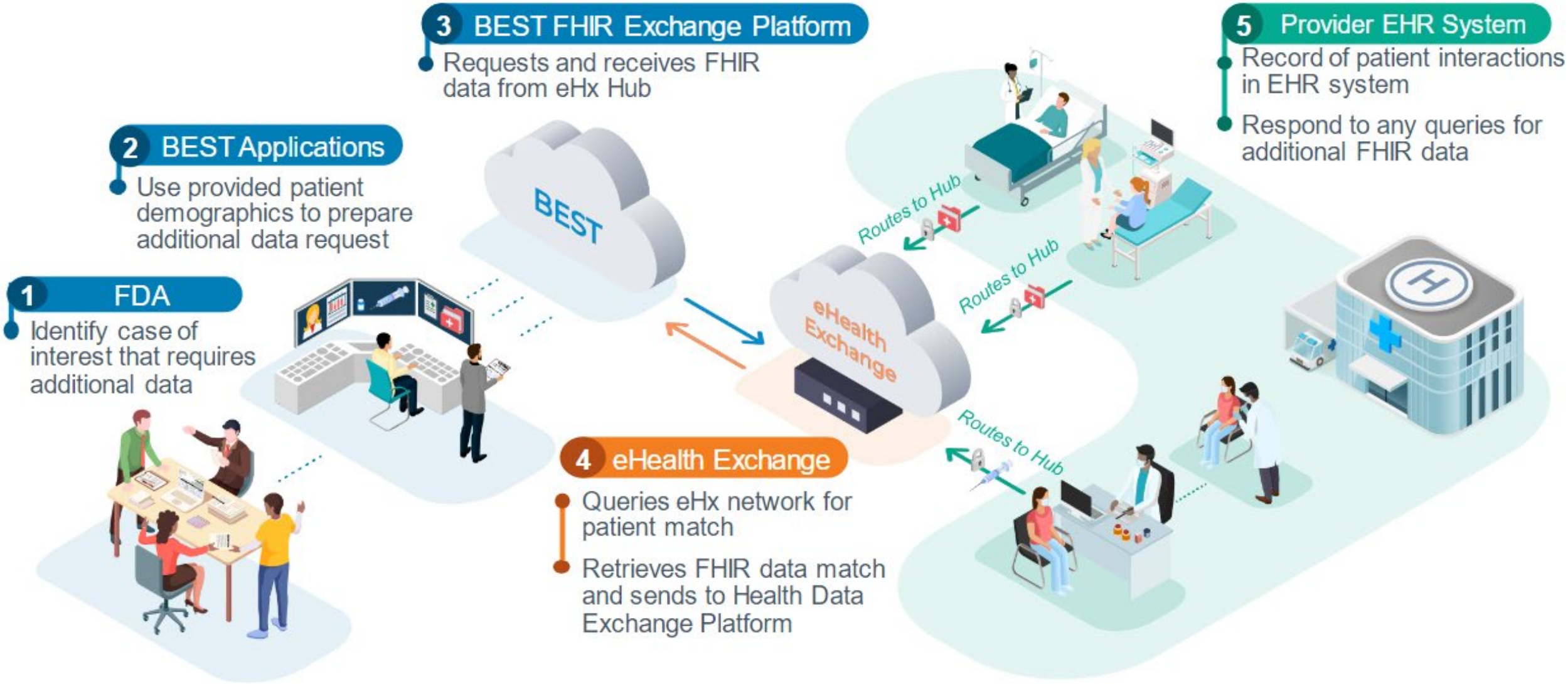
BEST Pilot Platform

BEST* Innovative Methods (IM) Initiative developed a Pilot Platform to address current challenges through AI and automation.



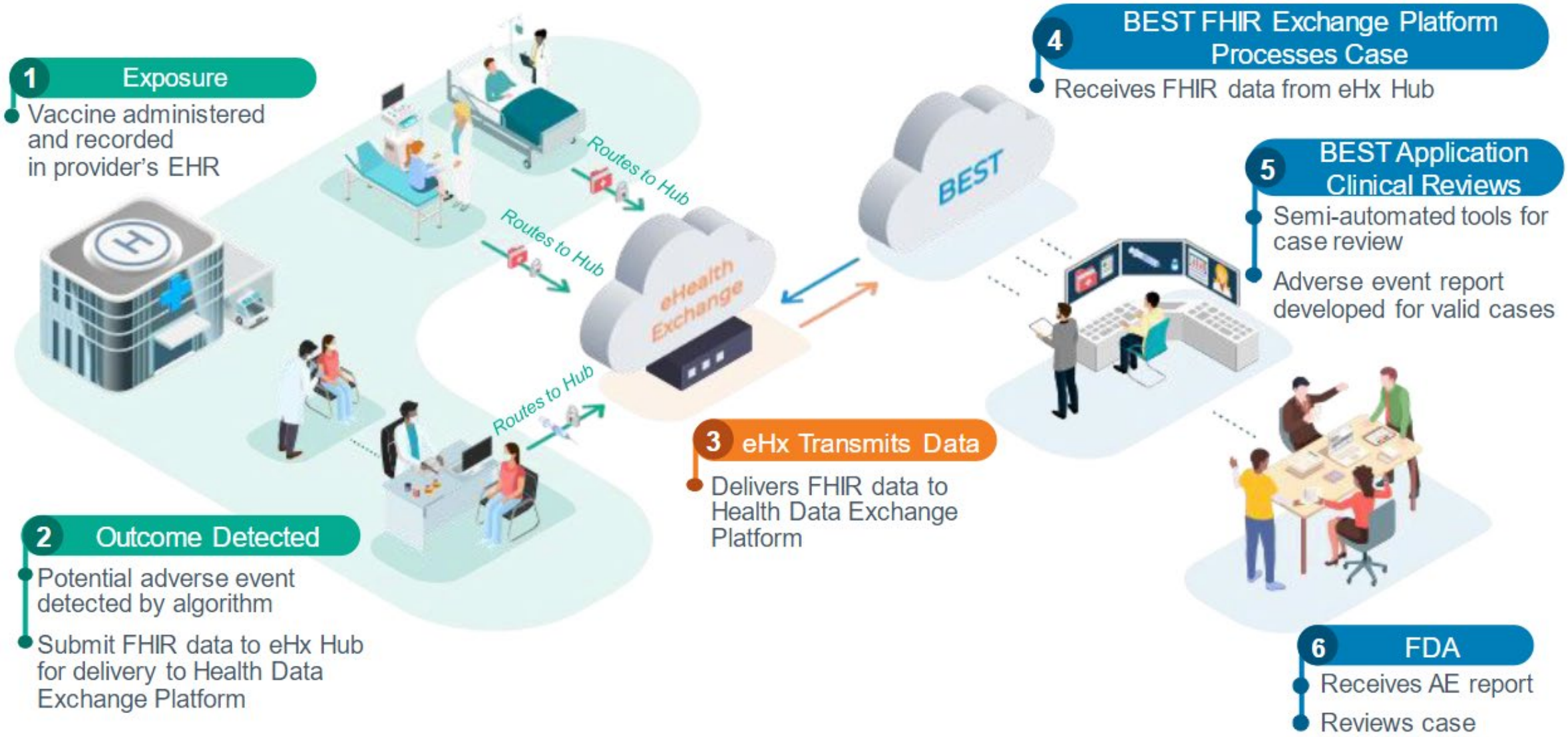
* ***BEST, Biologics Effectiveness and Safety*** ; ** eHx, eHealth Exchange

Validation (Pull) Use Case



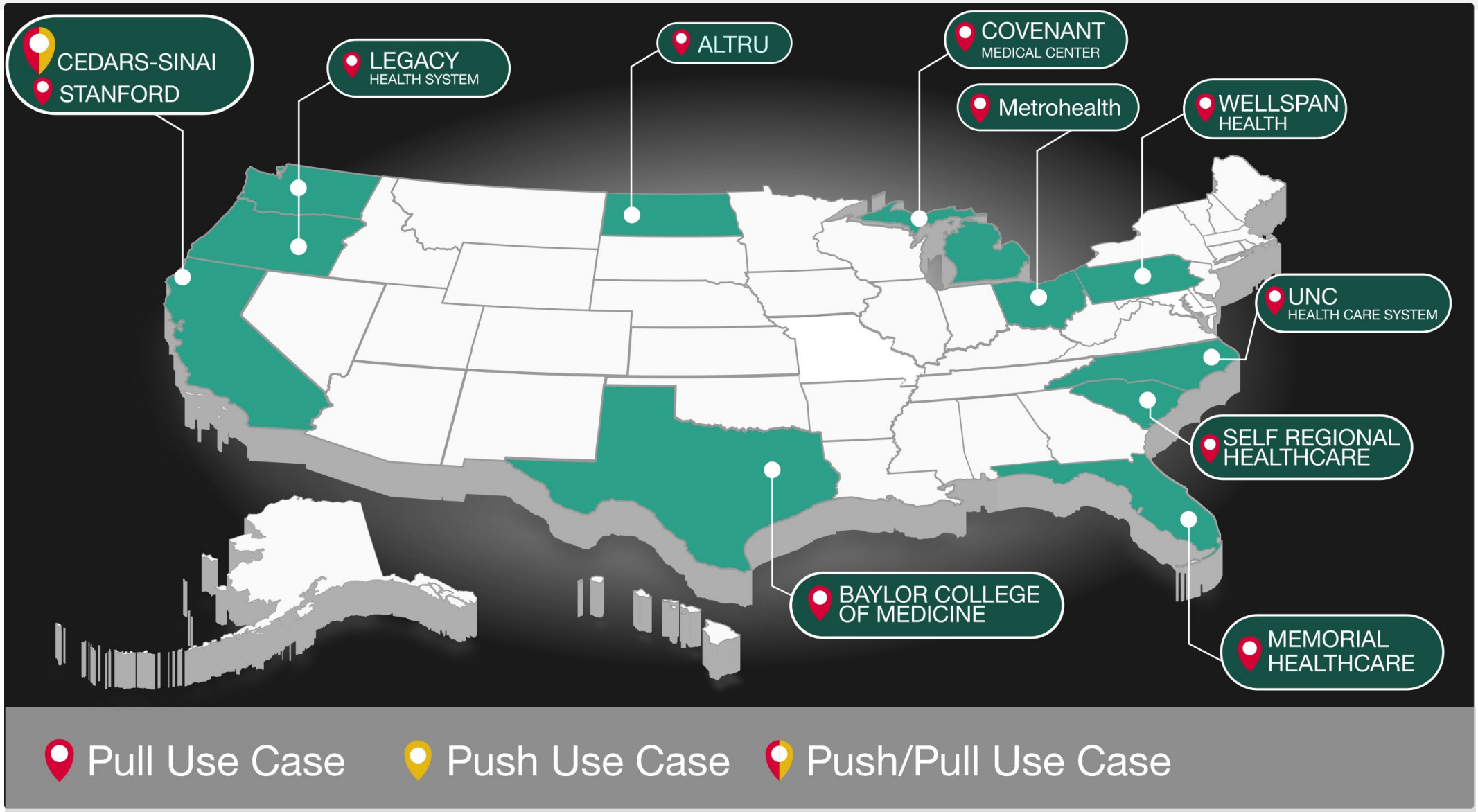
eHx, eHealth Exchange

Detection (Push) Use Case



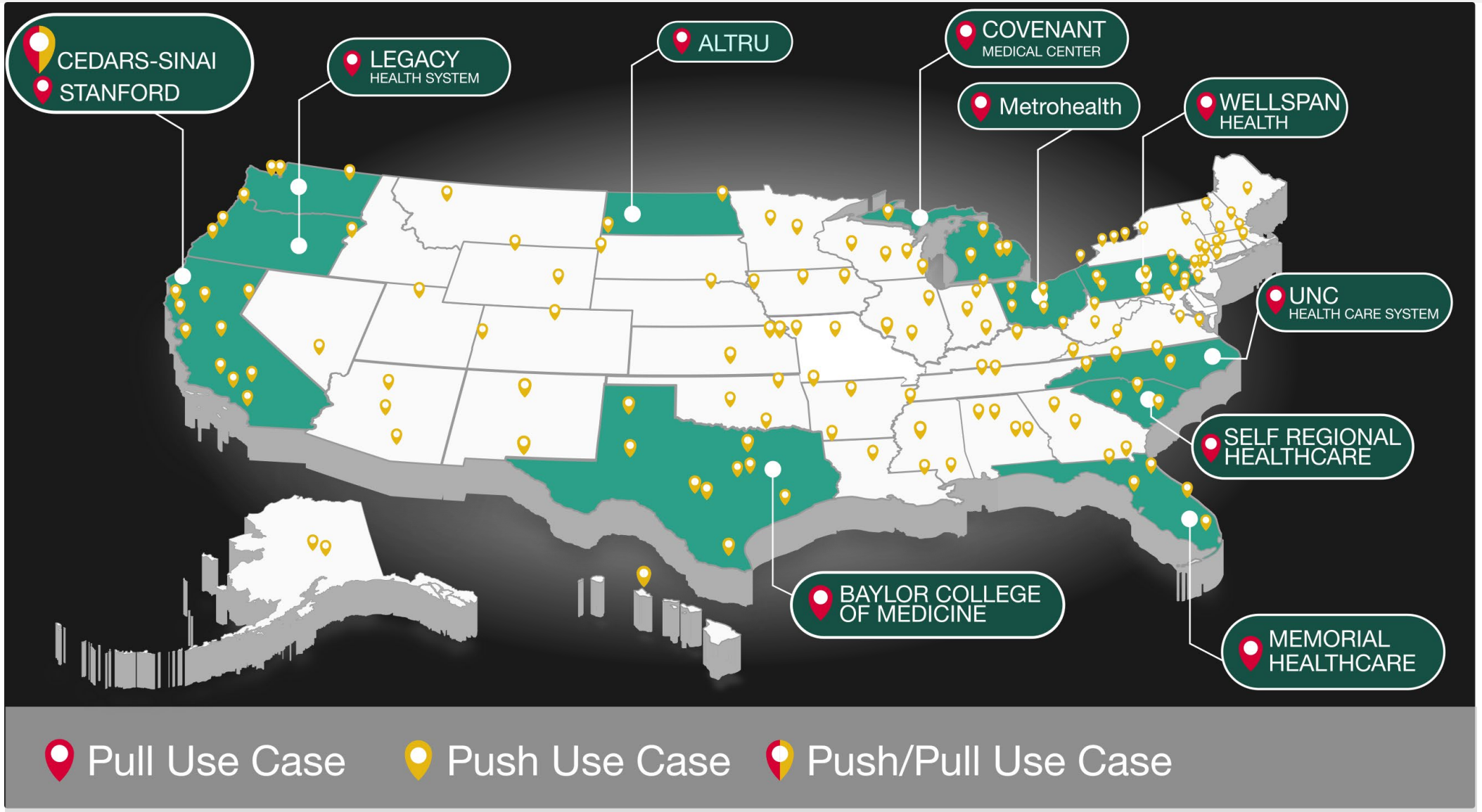
eHx, eHealth Exchange

Pilot Participants



https://ehealthexchange.org/participants/?participant_type=fda-pilot

Pilot Participants

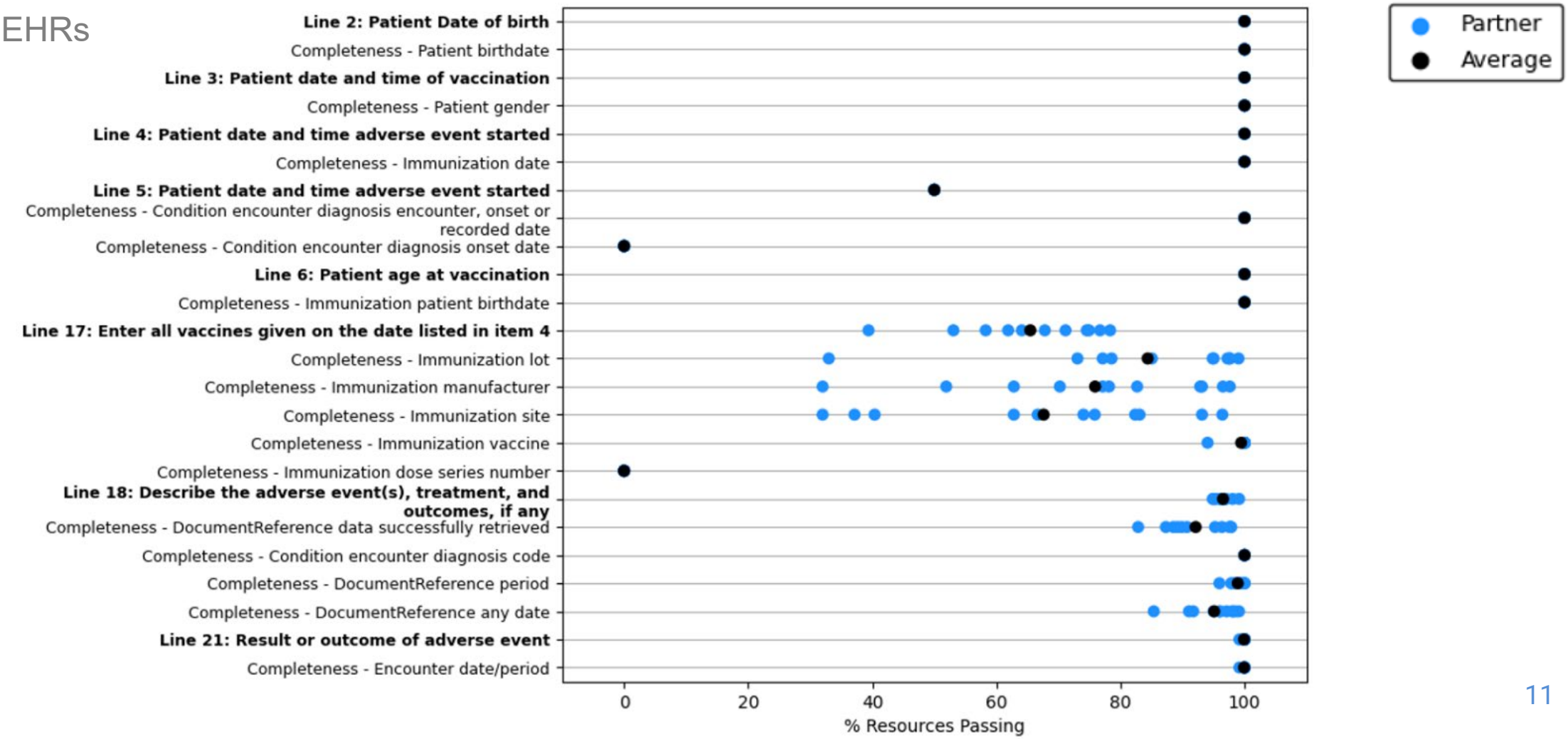


https://ehealthexchange.org/participants/?participant_type=fda-pilot

Pilot Results

- **271** post-vaccination AE were queried *
- Across **11** different health provider data partners (Epic EHRs)

* Patients EHRs



Conclusion and Summary

- For CBER's use case, **the overall data quality meets general requirements**, as partner's EHR HL7® FHIR® APIs are showing high adherence to USCDI data set
- **Variability** - even with same EHR vendor - in security authorization settings, required trail and error with individual partners
  - The team worked with EHR vendors to create a new policy that standardizes this process across partners to reduce the connection set-up time
- Important gaps include, **lack of inclusion in USCDI data set**, and **varying levels of completeness** across partners
- The BEST team continues to enhance the Platform infrastructure to enhance CBER's passive and active post-market surveillance capabilities:
  - improve our querying capabilities
  - efficiently federate AE detection logic
  - conduct evaluation and validation studies

Acknowledgement

FDA CBER	Barbee Whitaker, Artur Belov, Jane Mutanga, Brian Hively, Richard Forshee, Steven Anderson
IBM	Lance Jones, Matthew Deady, Brian Goodman, Haley Huang, Deepa Youssef, Kathryn Matto
eHx	Jay Nakashima, Eric Heflin, Mike Y and Mike M
Pilot Participant	• **CEDARS-SINAI HEALTH SYSTEM (early adopters)** • **VETERANS HEALTH ADMINISTRATION (VHA) (early adopters)** • WELLSPAN HEALTH • UNC HEALTH CARE SYSTEM • SOUTH BROWARD HOSPITAL DISTRICT DBA MEMORIAL HEALTHCARE SYSTEM • STANFORD HEALTH CARE • THE METROHEALTH SYSTEM • ALTRU HEALTH SYSTEM • BAYLOR COLLEGE OF MEDICINE • COVENANT MEDICAL CENTER • GREENWOOD COUNTY HOSPITAL BOARD DBA SELF REGIONAL HEALTHCARE • LEGACY HEALTH SYSTEM

References

- Vaccine Administrations From Unstructured Data in Medical Records Through Natural Language Processing
- Detection of allergic transfusion-related adverse events from electronic medical records
- FDA 2021 Science Forum: CBER BEST: Leveraging AI to Build an Automated Adverse Event Reporting System
- AI article about BEST C2 in FDA 2021 Science Forum July 2021
- Balloted BEST FHIR IG
- BEST FHIR IG on Interoperability Standards Advisory (ISA)
- BEST HL7 Case Study

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Veterans Health Information Exchange

VA Adverse Drug Event Reporting System (ADERS) Modernization

Todd Turner
Deputy Director, Technical
Veterans Health Information Exchange (VHIE)
Clinical Informatics Data and Management Office (CIDMO)
Office of Health Informatics (OHI)
Veterans Health Administration (VHA)
Todd.Turner@va.gov

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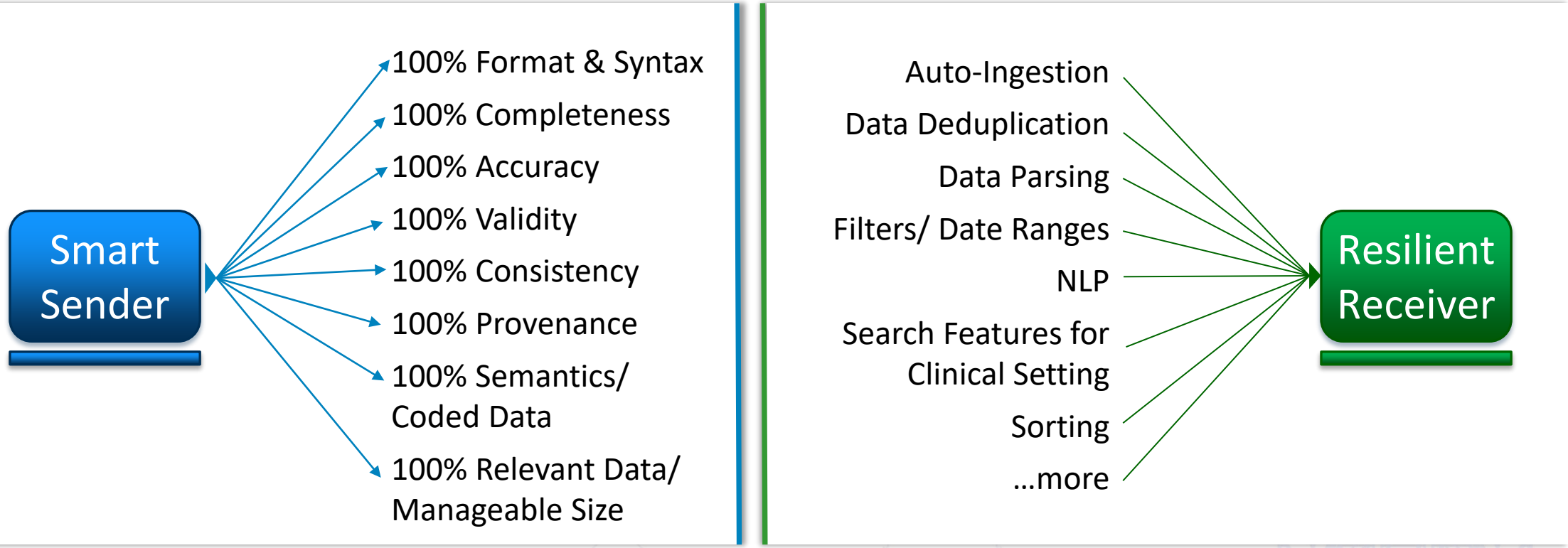
Agenda

- What the Veterans Health Information Exchange (VHIE) Strives to Achieve
- What We've Done
  - Collaboration Projects
  - Problem
  - Solution
- What We're Doing Today
  - Modernizing VA System Data Exchanges
  - Value to VA
  - Benefits of VA ADERS Modernization
- What We're Planning for the Future
  - Modernized Data Exchanges
  - Opportunities
- Q & A

What VHIE Strives to Achieve

To advance Data Usability, VA must be both a Smart Sender AND a Resilient Receiver



A Consolidated Clinical Document Architecture (C-CDA) or Fast Healthcare Interoperability Resource (FHIR) **on its own** cannot deliver the needed data usability.
Receivers (including VA) must provide resilient UI(s) to allow document data to be usable, computable, and actionable.

VHIE FHIR R4 Collaboration Projects

Proof of Concept

- May 2021 Collaboration Proposed
- September 2021 Executed successful end-to-end proof-of-concept test

Phase I: Push

- August 2022 Kickoff
- VA Adverse Event Reporting System (ADERS) modernized
- January 2023 Go Live VA **first** of 32 partners to cross finish line

Phase II: Query/Response

- July 2023 Kickoff of full bi-directional implementation

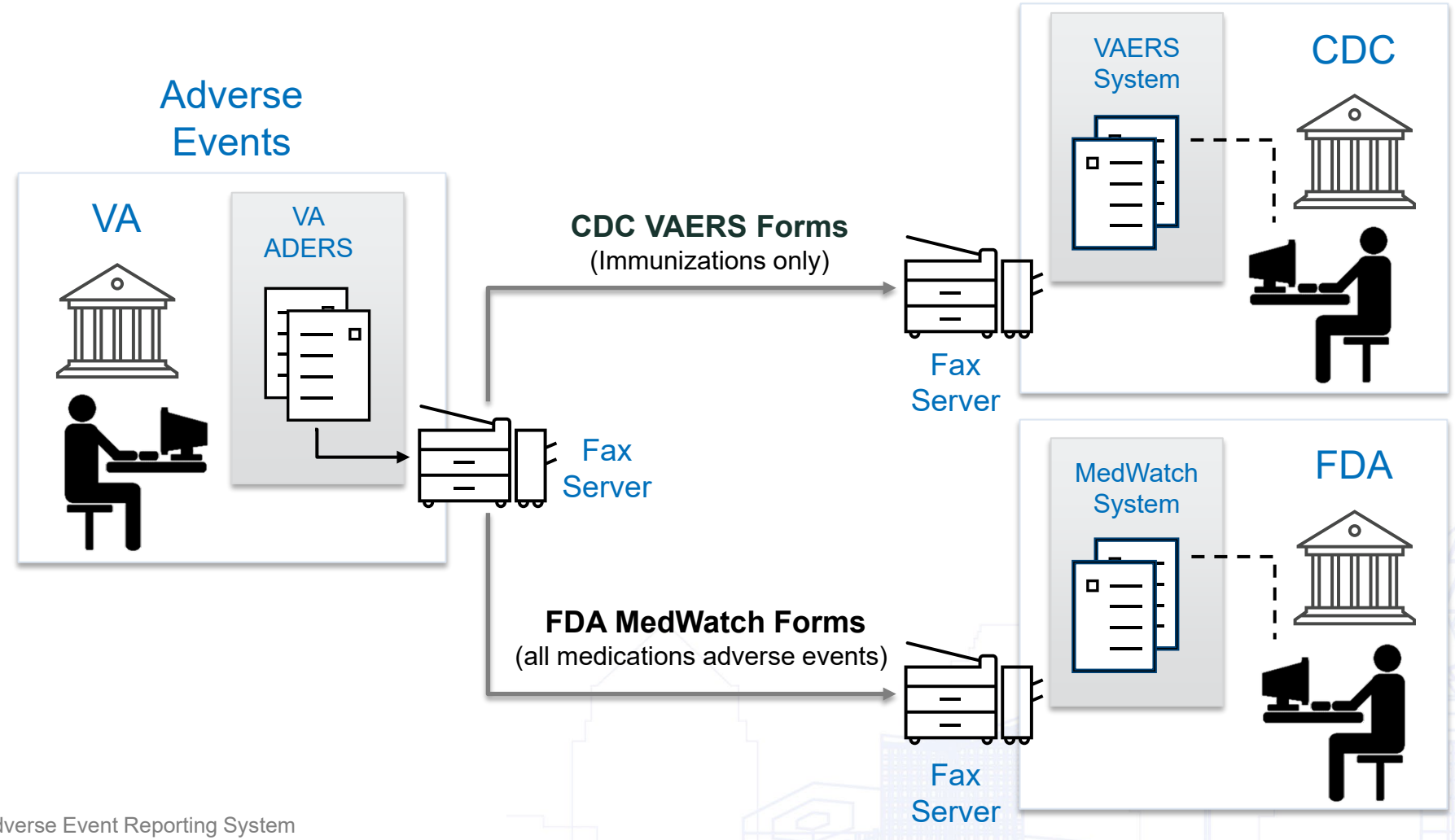
Phase III: CQL Prototype

- Spring 2024 Kickoff FDA's Myocarditis Pericarditis CQL Query

eHx = eHealth Exchange
FDA = Food and Drug Administration
HL7 FHIR R4 = Health Level Seven International (HL7) Fast Healthcare Interoperability Resources Release #4
CQL = Clinical Quality Language

Problem: High Failure, Manual Process

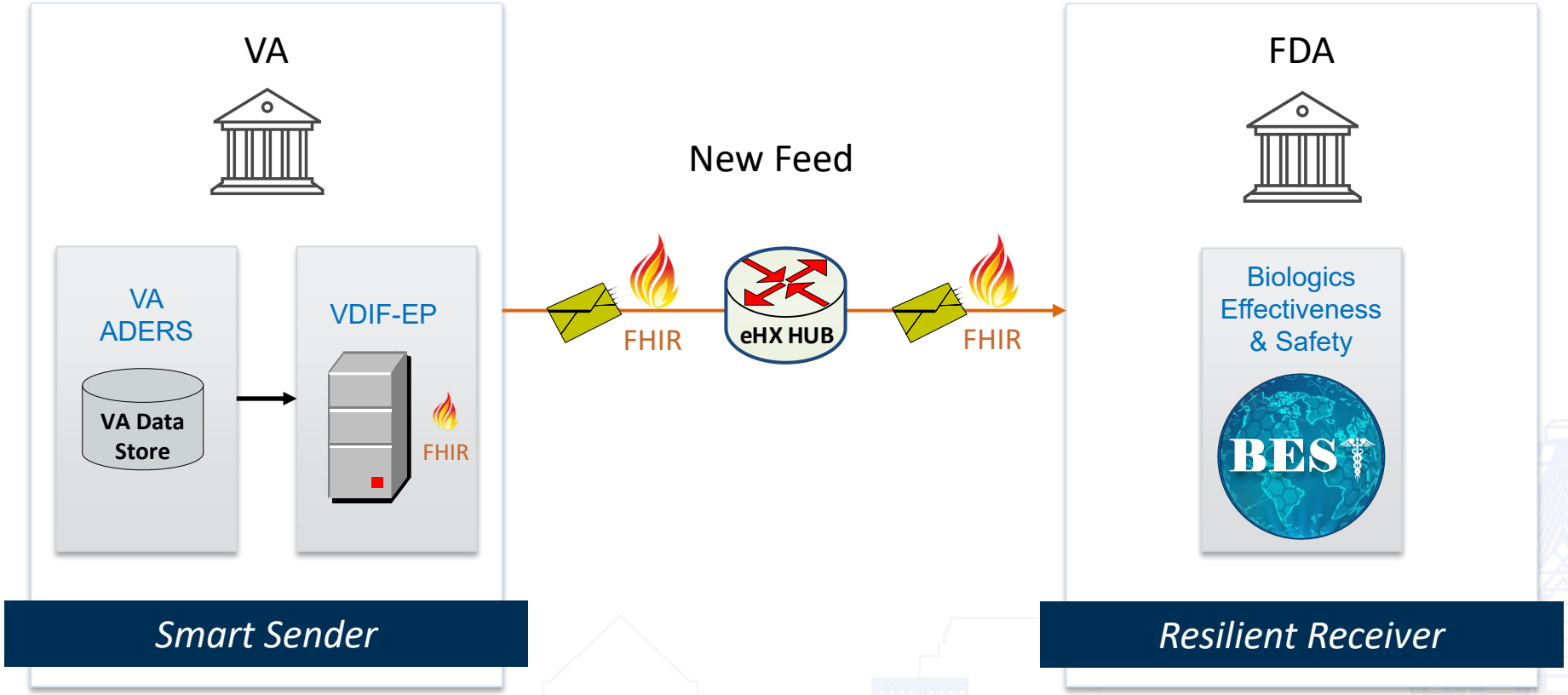
VA ADERS Fax Transmission to Centers for Disease Control and Prevention (CDC) & Food & Drug Administration (FDA)



VAERS = Vaccine Adverse Event Reporting System

Solution: Modernize VA Adverse Drug Event Reporting (ADERS) System

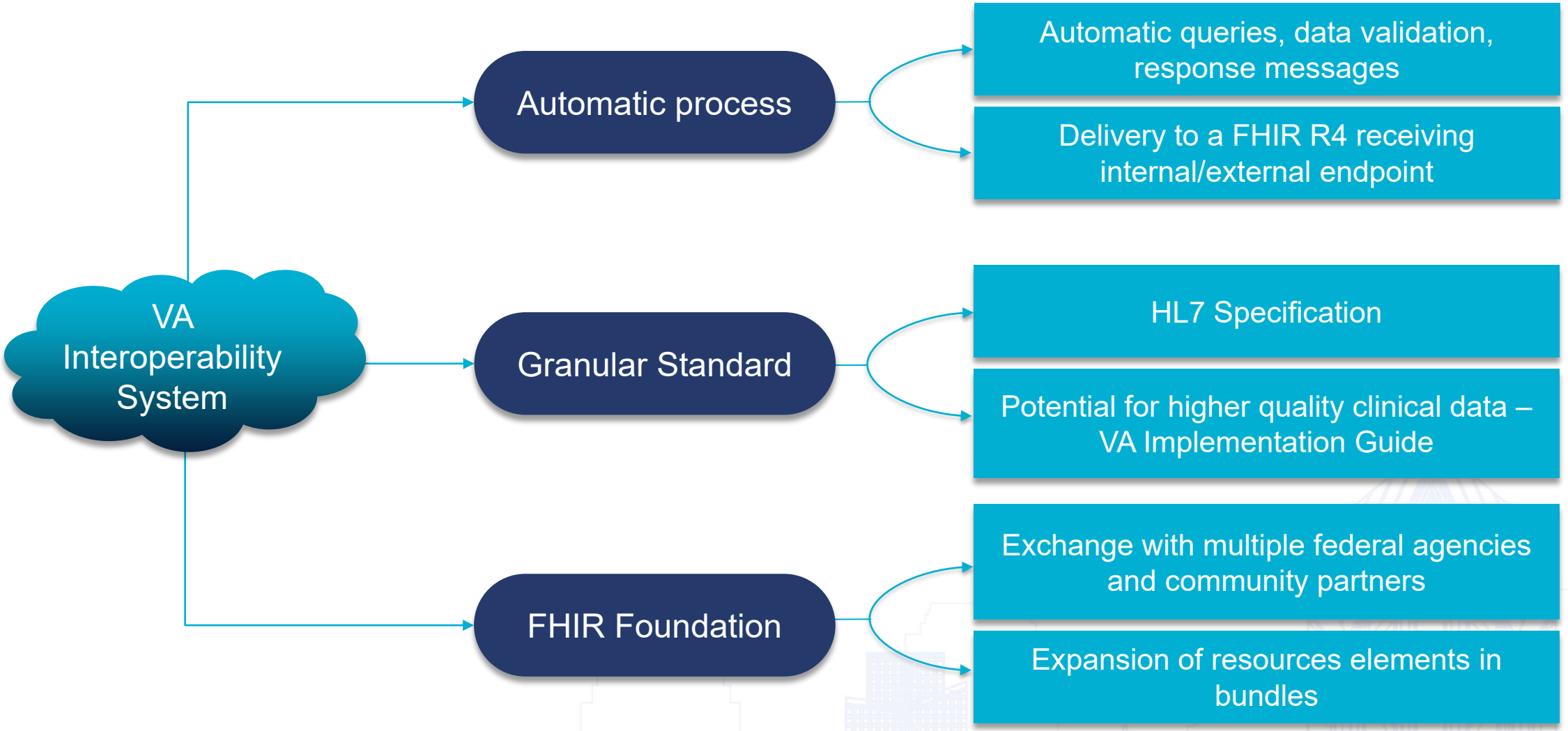
COVID-19 Immunizations Adverse Event Report



Automatic, simple, reliable, and reduces potential for human and fax transmission errors

eHx = eHealth Exchange
VDIF-EP = Veterans Data Integration and Federation Enterprise Platform
FHIR = Fast Healthcare Interoperability Resources

Modernizing VA System Data Exchanges

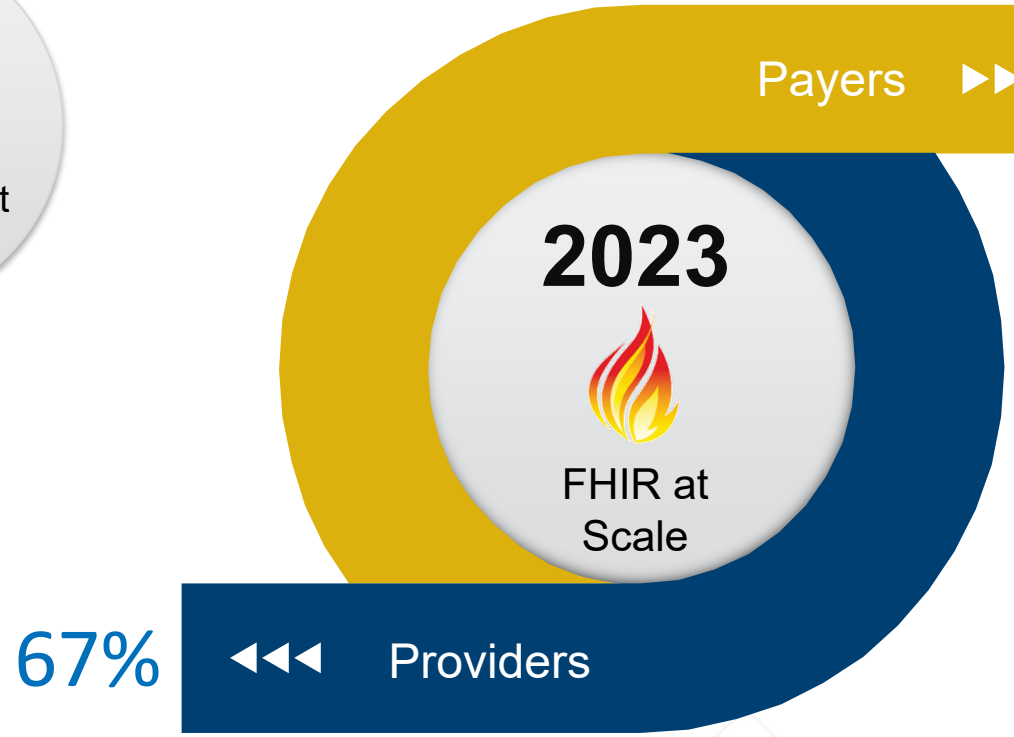


FHIR = Fast Healthcare Interoperability Resources
HL7 = Health Level Seven International

Moving VA to be both a Smart Sender and a Resilient Receiver

Value to VA

2021
24%
FHIR at Scale



Modernization!

- Health IT industry is moving toward automated FHIR exchanges.
- Provides low-cost opportunity to modernize and improve interoperability of VA systems.
- 61% of Payers and 67% of Providers expect their respective organizations to use Application Programming Interfaces (APIs) at scale by 2023.

FHIR = Fast Healthcare Interoperability Resources

(Engine Group survey commissioned by Change Healthcare, 2021)

Benefits of VA ADERS Modernization

Efficiency

- ✓ Automated electronic transmission versus fax
- ✓ Reduced human resource component receiving faxed reports

Accuracy

- ✓ Reduce/eliminate human error on re-entering data from faxed reports

Automation

- ✓ Via a graphical user interface (GUI) for ease of managing/automating data transfers

Add metrics

- ✓ Success/Failure at a minimum

Opportunity

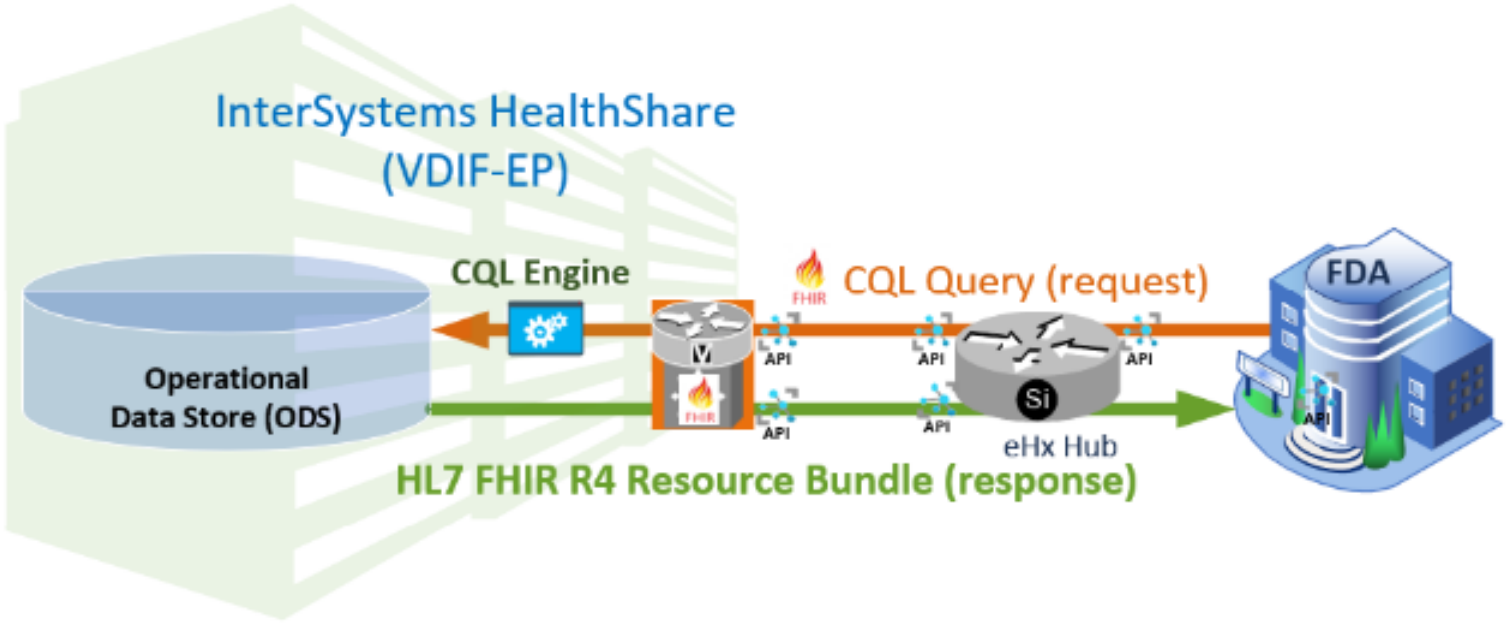
- ✓ Develop processes with FDA/CDC to accept new file format

CDC = Centers for Disease Control and Prevention
FDA = Food and Drug Administration

(Von Moore, VHA Program Specialist Pharmacist for VA ADERS, 2022)

Future (2024) CQL Automated Data Exchange

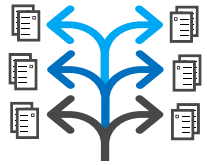
Asynchronous – Reduces traffic/processing burden on all three systems (FDA/eHx/VHA)
Test Control Group – Request/Response COVID-19 ADE clinical domains (Phase II Pilot)



FDA = Food and Drug Administration
HL7 FHIR R4 = Health Level Seven International (HL7)
Fast Healthcare Interoperability Resources Release #4
CQL = Clinical Quality Language
eHx = eHealth Exchange

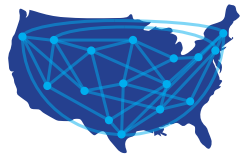
Opportunities

The established FHIR foundation provides the VA *(VA ADERS/PBM)* with numerous opportunities to:



Expansion of Adverse Events Reporting

- Expand to all Immunizations to FDA
- Expand to CDC for Immunizations
- Expand to all adverse drug events



Expansion to Other Federal Agencies

- Minimal code customization
- Code reuse
- Some policy updates
- Nominal implementation cost for expansion
- Leverage VDIF work from other projects

Adopt and Fund FHIR Additional Projects

- Increase efficiency
- Reduce Risk
- Free up resources
- Minimal effort and low cost to evolve

PBM = Pharmacy Benefits Management Services
VDIF = Veterans Data Integration and Federation

References

- Jason, C. (2021, April 06). *API Adoption Slow, Widespread FHIR Uptake Expected by 2024*. Retrieved from EHR Intelligence: https://www.ehrintelligence.com/news/api-adoption-slow-widespread-fhir-uptake-expected-by-2024#:~:text=April%2006%2C%202021%20-%20Only%2024%20percent%20of,from%20the%20Engine%20Group%20commissioned%20by%20Change%20Healthcare.

Exchange Pilot for Automation of Vaccine Adverse Event Reporting

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Cedars-Sinai Experience with the FDA/IBM/eHealth Exchange Pilot

Ray Duncan, MD, FAAP, FAMIA
Executive Director, Technology R&D
Enterprise Information Services
Cedars-Sinai Health System
ray.duncan@cshs.org

With thanks to:
Renier Estiandan and Matt Sonesen, EIS Technology Architects

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Legacy Process - Manual Reporting (as implemented at Cedars-Sinai)

- Vaccine reactions documented in the EMR are sent to pharmacy on a daily report
- Pharmacy manually reports significant reactions via the FDA VAERS web form
- Majority of 195 documented reactions in the two year period starting December 2020 were minor (headache, sore arm, etc.).
  - 5 out of 195 reactions included anaphylaxis, only these were reported to FDA.
  - Serious adverse reactions that do not occur immediately after the injection (e.g. myocarditis, thrombosis) rely on clinician detection/correlation.
  - If not associated with the vaccine administration and documented in the EMR, adverse events are not going to be manually reported to the FDA by CSHS.
- Based on the VAERs form, FDA requests the patient chart by phone call, email or FAX

FDA On-Line VAERS Form

VAERS Vaccine Adverse Event Reporting System
www.vaers.hhs.gov

Adverse events are possible reactions or problems that occur during or after vaccination.
Items **2, 3, 4, 5, 6, 17, 18** and **21** are **ESSENTIAL** and should be completed.
Patient identity is kept confidential. Instructions are provided on the last two pages.

INFORMATION ABOUT THE PATIENT WHO RECEIVED THE VACCINE (Use **Continuation Page** if needed)

1. Patient name: (first) (last)
Street address:
City: State: County:
ZIP code: Phone: ( ) Email:

2. Date of birth: (mm/dd/yyyy) **3.** Sex: ☐ Male ☐ Female ☐ Unknown

4. Date and time of vaccination: (mm/dd/yyyy) Time: hh:mm ☐AM ☐PM

5. Date and time adverse event started: (mm/dd/yyyy) Time: hh:mm ☐AM ☐PM

6. Age at vaccination: Years Months 7. Today's date: (mm/dd/yyyy)

8. Pregnant at time of vaccination?: ☐ Yes ☐ No ☐ Unknown
(If yes, describe the event, any pregnancy complications, and estimated due date if known in item 18)

9. Prescriptions, over-the-counter medications, dietary supplements, or herbal remedies being taken at the time of vaccination:

10. Allergies to medications, food, or other products:

11. Other illnesses at the time of vaccination and up to one month prior:

12. Chronic or long-standing health conditions:

INFORMATION ABOUT THE PERSON COMPLETING THIS FORM

13. Form completed by: (name)

Relation to patient: ☐ Healthcare professional/staff ☐ Patient (yourself) ☐ Parent/guardian/caregiver ☐ Other:

Street address: ☐ Check if same as item 1
City: State: ZIP code:

INFORMATION ABOUT THE FACILITY WHERE VACCINE WAS GIVEN

15. Facility/clinic name:
Fax: ( )
Street address: ☐ Check if same as item 13

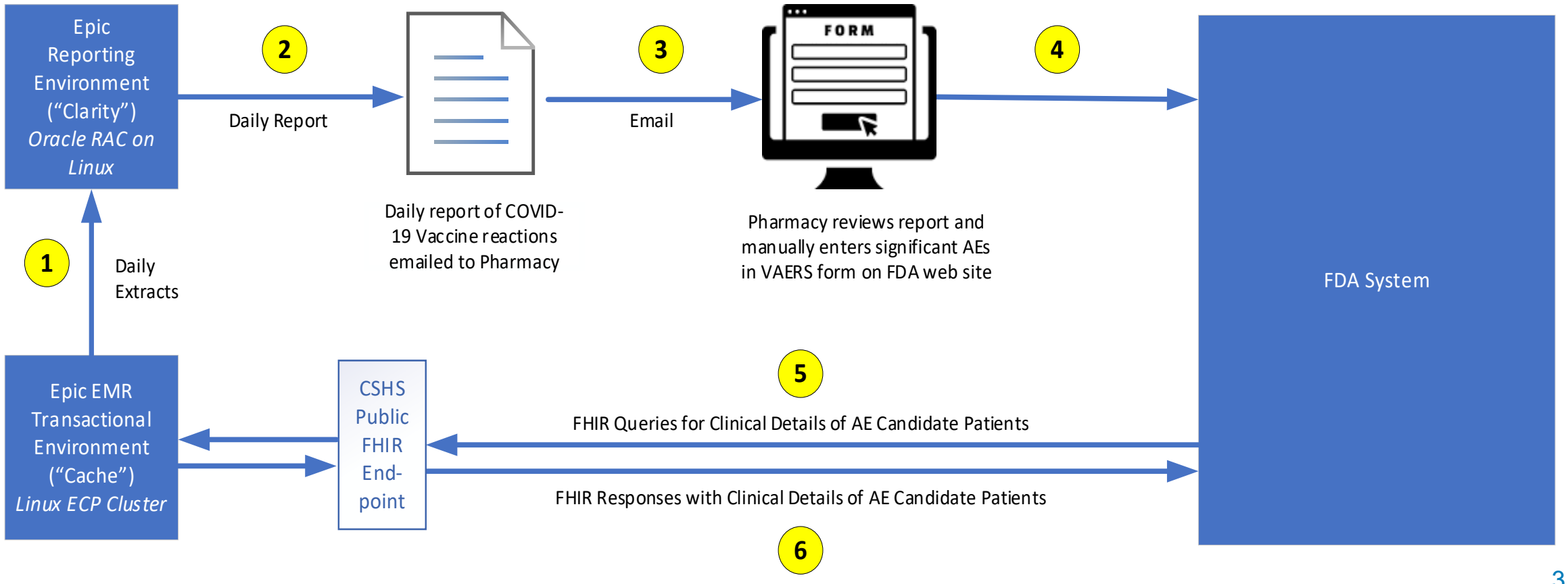
16. Type of facility: (Check one)
☐ Doctor's office, urgent care, or hospital
☐ Pharmacy or store
☐ Workplace clinic
☐ Public health clinic
☐ Nursing home or senior living facility

FDA Pilot Phase 1 "Pull" (as implemented at Cedars-Sinai)

- Vaccine reactions documented in the EMR are reported to pharmacy on a daily Clarity report.
- Pharmacy manually reports significant reactions to FDA using the online VAERS form on the FDA web site.
- For testing purposes we also supplied the FDA directly with a list of patients with adverse effects based on queries of the EMR (including reactions that were not reported by pharmacy)
- FDA retrieves the clinical information via eHealth Exchange using a Open.Epic FHIR Client ID and the Cedars-Sinai public endpoint.
- FDA imports problem list, vaccination history, medications, clinical notes, etc. to the FDA BEST system for semi-automated case review.
- Valid Adverse Events are summarized in an FDA internal report.

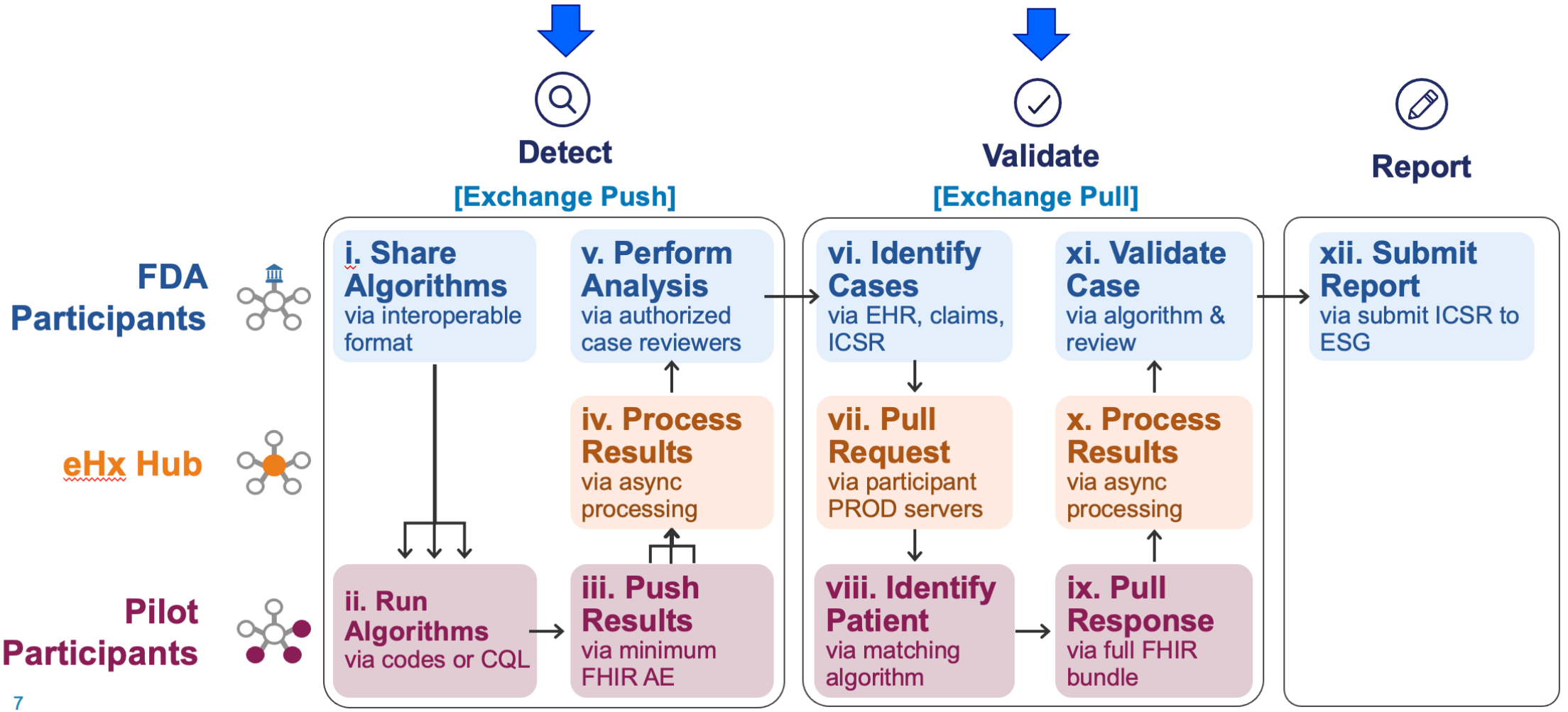
Pilot Phase 1 "Pull" data flow diagram (as implemented at C-S)

Note: "FDA Team" as used here is shorthand for all contributors from FDA, eHealth Exchange, and IBM



BEST Exchange Pilot Phase 2 – Push and Pull Use Case

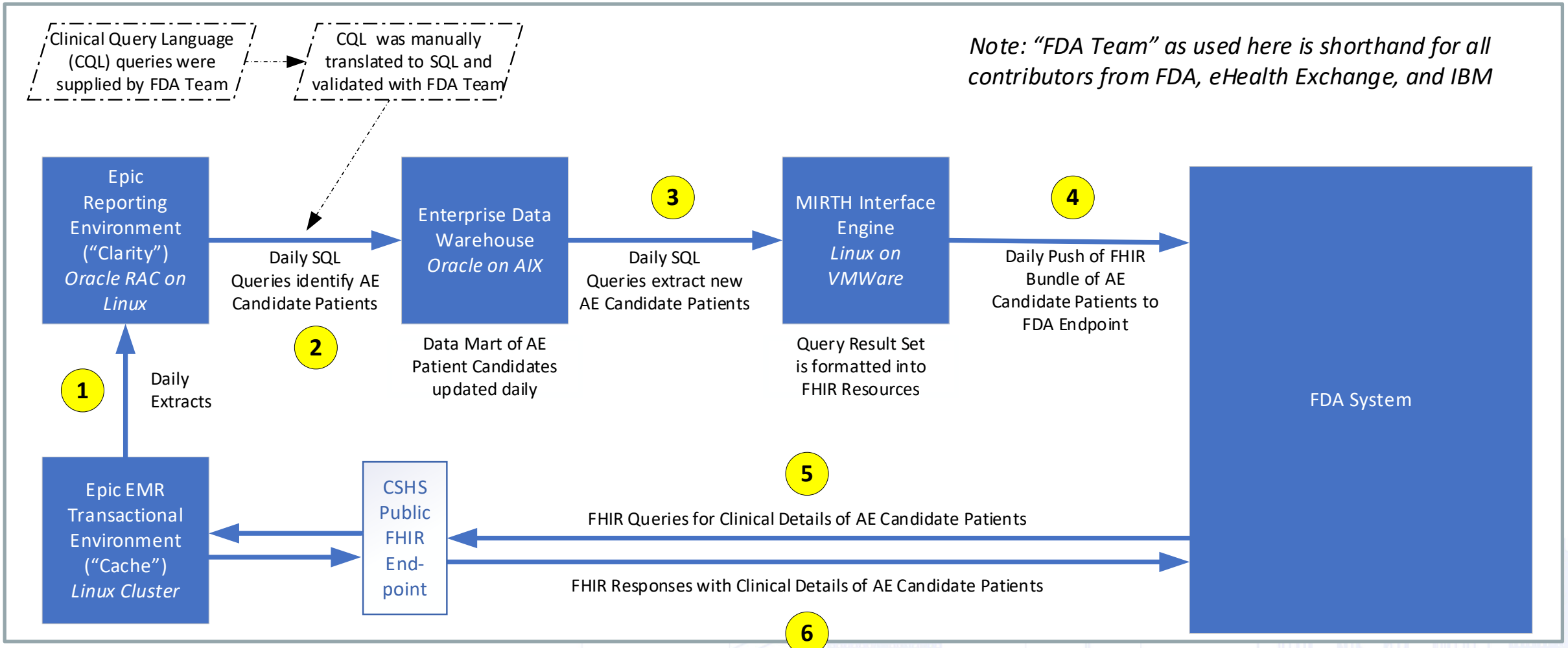
- **Detection** and **validation** (i-ix)



FDA Pilot Phase 2 “Push and Pull” (as implemented at C-S)

- Scheduled SQL query in the Epic reporting environment executes a patient selection algorithm translated from CQL. Query criteria include COVID vaccination types and dates, diagnosis codes, temporal relationships of vaccination to diagnoses, lab results, etc.
- Query results are marshalled into a staging table in the enterprise data warehouse.
- MIRTH interface engine accesses the staging table and formats a FHIR JSON bundle of patient identifiers and pushes it to the eHx endpoint which relays it to the FDA system.
- FDA ”pulls” patient chart information via eHealth Exchange using a Open.Epic FHIR Client ID and the Cedars-Sinai public endpoint.
- FDA imports problem list, vaccination history, medications, clinical notes, and other clinical information to the FDA BEST system for semi-automated case review.
- Valid Adverse Events are summarized in an FDA internal report.

Pilot Phase 2 "Push & Pull" Data Flow Diagram (as implemented at C-S)



Problems and Lessons Learned

- Manual translation of the CQL to SQL required close collaboration with the FDA/IBM/eHx team.
  - In the absence of EMR vendor support for direct translation of CQL to a locally supported DBMS query language, a CQL-based approach will be difficult to scale.
- Several candidate patients in our early trial queries had Break-the-Glass (BTG) protection on their records, which would block the retrieval of records from the CSHS public FHIR endpoint.
  - Remedied by associating the FHIR Client ID with a service account that can bypass BTG.
- The initial testing of the database queries uncovered some issues with the algorithm:
  - Some patients did not get a lab confirmation within the defined time window.
  - Ambulatory lab results that were filed in the EMR post-discharge could also fail the query criteria.
  - Observation or ED patients didn't meet the inpatient criteria on the lookbacks.
  - Patients who previously had myocarditis/pericarditis caused false positives.
- Query issues were resolved through discussions with the FDA/IBM/eHx team and optimization.

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THANK YOU FOR YOUR PARTICIPATION

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