CBER Biologics Efficacy and Safety Sentinel (BEST) Program #2

Development of New and Innovative Methods for Automated Reporting for CBER-Regulated Biological Products

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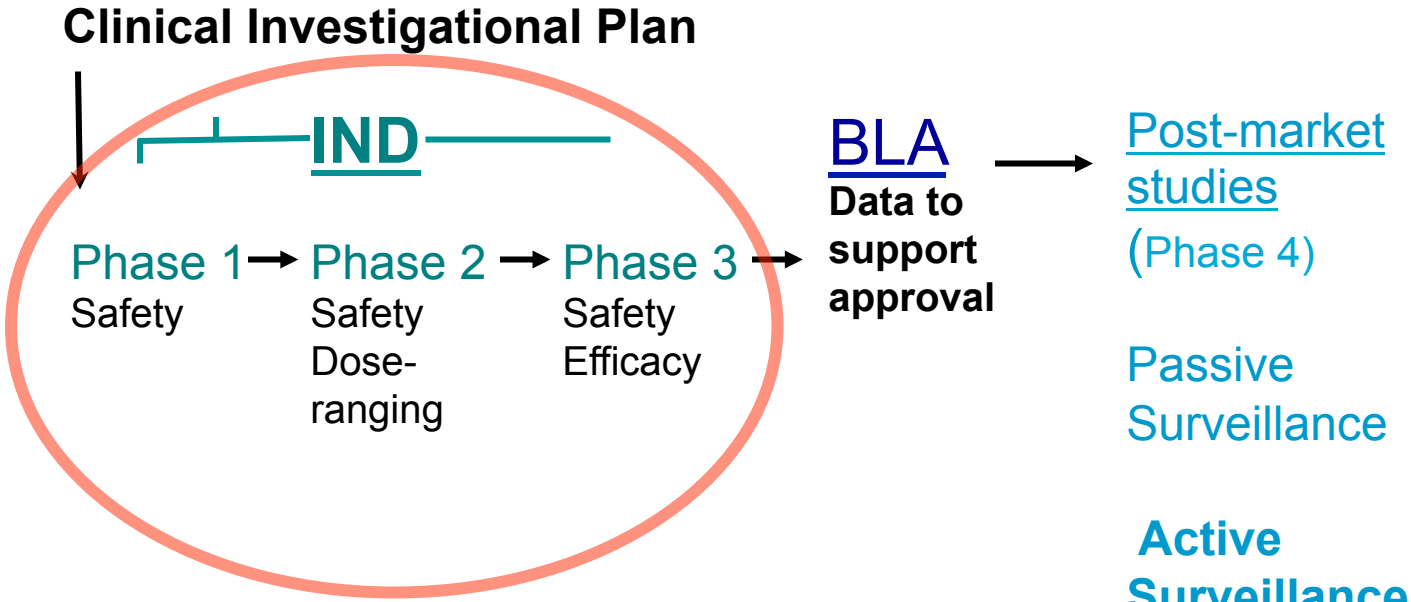
Typical Biologics Product Approval Lifecycle



IND: Investigational New Drug Application
BLA: Biologics License Application

BEST #2 – Two Major Program Goals: Regulatory Perspective

I. Develop Infrastructure to improve the quality (accuracy and predictive value) of active post-market (PM) surveillance beyond what is available solely from ”big data” resources based on billing codes. (FDAAA 2207)

1. Exposures
2. Outcomes
3. Initial emphasis on blood transfusion (hemovigilance)*

* Blood components are established products. Pre-market review is based on adequacy of manufacturing procedures, not efficacy)

BEST #2 – Program Goals: Regulatory Perspective

II. Increase the efficiency (reduce the burden) of PM surveillance reporting

PM e-reporting of product adverse events (AE) to FDA by manufacturers now required for most FDA-regulated products (passive); MEDWatch/FAERS/VAERS

- Many reports, variable quality

PM Reporting not required for blood transfusion at this time.

- Voluntary reporting to FDA essentially non-existent
- US hemovigilance (public and private) very challenging (no national healthcare system; poor data interoperability
- Limited resources for hemovigilance at institutional level
- Adverse events are rare and have diagnostic complexity

Enhanced exposure and Outcome (Computable Phenotype) Development

- Outcome and Diagnostic codes alone (claims, EHR)
- Constellations of available structured data (enhanced claims, EHR)
- Computable phenotypes - available structured data + data mined from clinical and nursing notes, radiology reports, non-structured labs
- **Case validation by clinical review of charts (semi-automated)**

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BEST2 - Workstream 1/5

1. Improved sensitivity and granularity of **transfusion exposures** compared to claims data alone

   Lead: Columbia University

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BEST2 - Workstream 2/5

Iterative NLP-based development of computable phenotypes (CP) reflecting: **Enhanced characterization of Post-transfusion Transfusion-Associated Circulatory Overload (TACO)**

Lead: Stanford University

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BEST2 - Workstream 3/5

Iterative NLP-based development of computable phenotypes (CP) reflecting: **Post-transfusion Sepsis (PTS)**

Regenstrief Institute

FDA U.S. FOOD & DRUG ADMINISTRATION

BEST2 - Workstream 4/5

Infrastructure to support interoperability within BEST (and potentially more broadly) through harmonized use of CLARITY NLP platform to support more efficient iterative NLP studies

Lead: Georgia Tech Research Institute (GTRI), Columbia University

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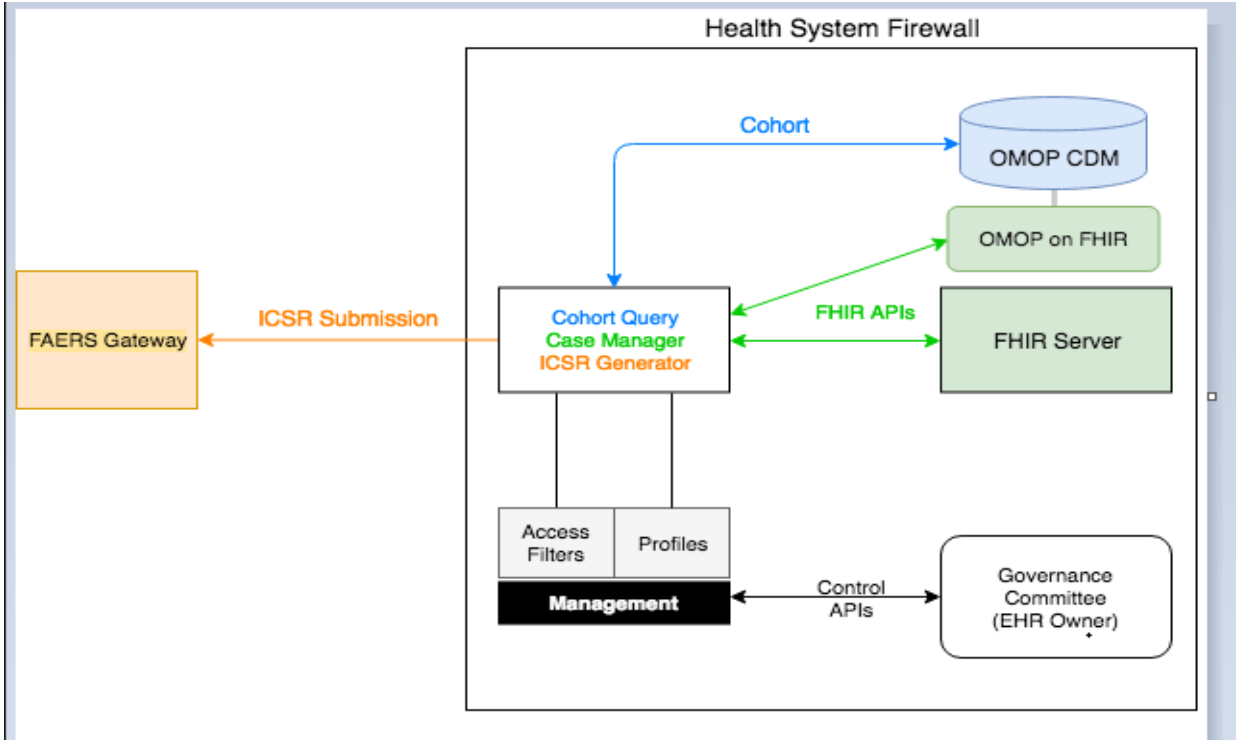
BEST2 - Workstream 5/5

Building infrastructure to support **nationwide scale-up of CP-based case identification and automated report generation**

Lead: Georgia Tech Research Institute

Adverse Event Surveillance OHDSI Platform (AESOP)



BEST-2 Future Challenges

- Time stamps derived from EHR for events: hour/minute/ (second?)
- Iterative CP development processes are of high value, but can efficiency be improved? (CBER regulates many unique products with unique AE)
- Collaboration with EHR vendors, HL7 FHIR to support eventual scale-up

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