ENGELBERG CENTER for Health Care Reform at BROOKINGS

Sentinel Initiative Public Workshop

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State of CBER's Mini-Sentinel Activities

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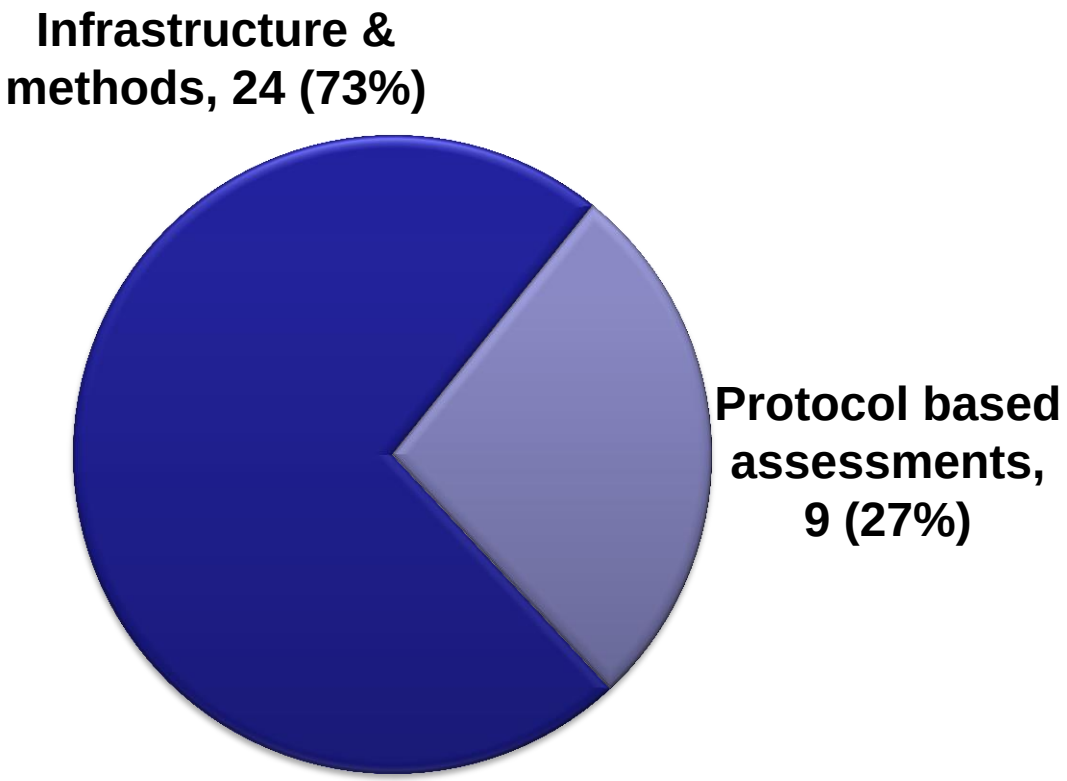
Plan for Talk

- A brief 3.3 year review (9/2010 – 1/2014)
  - Project overview
  - Steps taken to ensure rigor and transparency
  - Select accomplishments to date
  - What impact has Mini-Sentinel had at CBER?

- Where are we headed from here?
  - Strategic priorities

Total CBER Projects by Type

(9/2010 – 1/2014)



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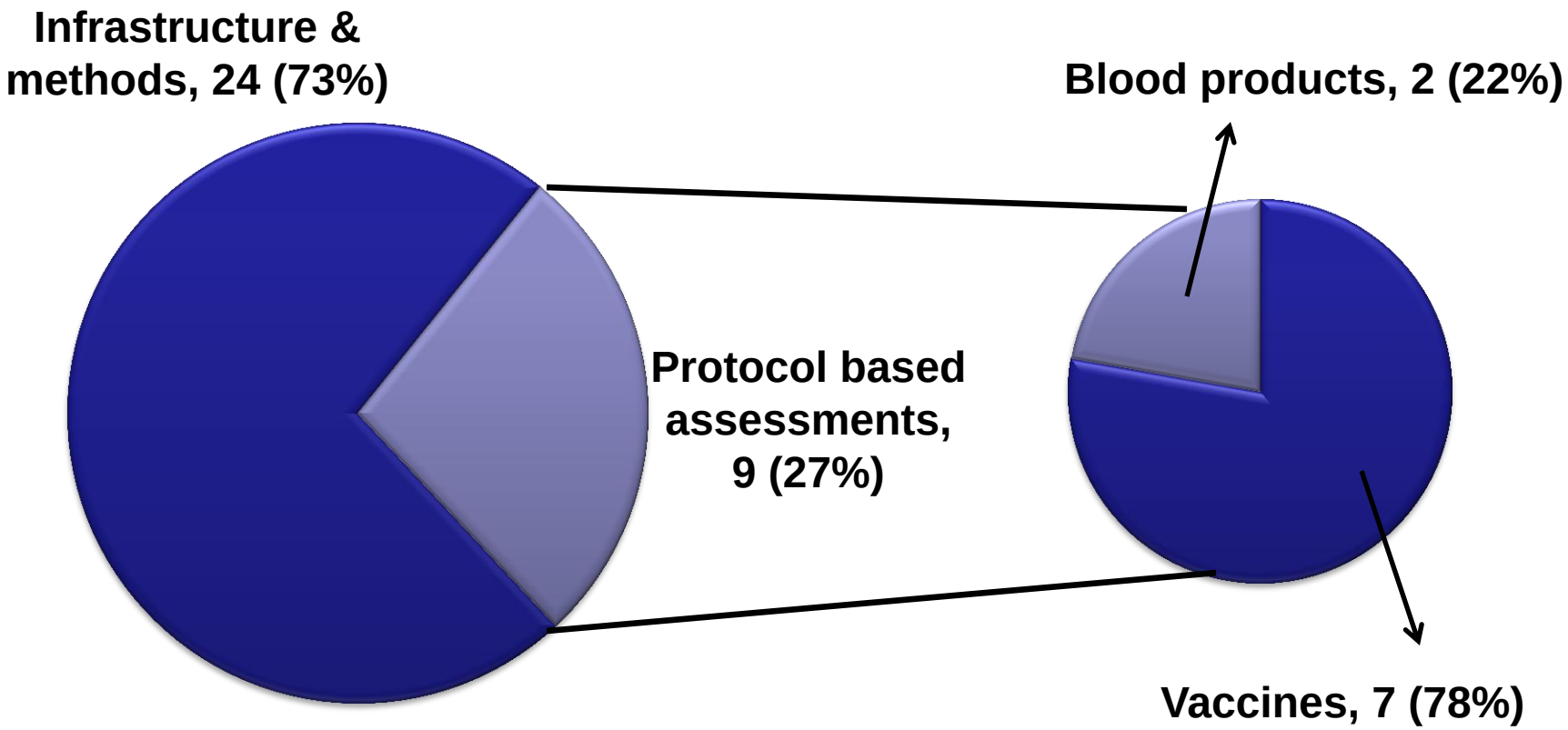

CBER Study Timelines

	Surveillance Assessment	Anticipated Protocol Posting Date	Anticipated Final Report Posting Date
1	Rotavirus vaccines and intussusception	Posted 10/24/2011	Posted 6/14/2013
2	Gardasil vaccine and venous thromboembolism	Posted 3/30/2012	Spring 2015
3	Influenza vaccines and febrile seizures	Posted 1/25/2013	Spring 2014
4	Influenza vaccines and birth outcomes	Posted 2/25/2013	TBA
5	Influenza vaccine safety sequential analysis	Posted 8/2/2013	TBA
6	Influenza vaccines and pregnancy outcomes	Posted 9/18/2013	TBA
7	Thromboembolic events after immunoglobulin administration	Posted 9/20/2013	TBA
8	Prevnar 13 vaccine and Kawasaki Disease	Spring 2015	TBA
9	TRALI after platelets, plasma, and red blood cells	TBA	TBA

http://mini-sentinel.org/assessments/medical_events/default.aspx

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Taking Cues from Gold Standard Methods

Clinical Trials	Sentinel Protocol Based Assessments
Clear inclusion/exclusion criteria to meet study objectives	Assessment of suitability of fit between data source and scientific question; carefully crafted study cohorts
Full clinical narratives to support safety assessment	Access to medical records to validate exposures and outcomes
Randomization to ensure balance between study groups	Use of observational analyses that minimize bias (e.g. self-controlled)
FDA review and approval of endpoints, analyses and protocols	FDA serves as co-investigator and co-develops analyses, study protocol, final report
Registration @ clinicaltrials.gov	Posting @ minisentinel.org
	Public comment period

Select Accomplishments to Date

- **Infrastructure and methods**
  - Strengthened core data sources by adding vaccine registries, birth certificate and fetal death data
  - Expanding surveillance to intravenous and inpatient medical products by incorporating hospital data
  - Developing new methods to identify unexpected adverse events
- **Protocol based assessments**
  - Expanded from vaccines to blood derived products and blood components
  - Piloting near real time surveillance for 2013-14 influenza season
  - Launched 2 studies to build novel pregnancy safety capabilities

Mini-Sentinel's Impact on CBER

- Created independent source of population-based data for FDA
  - Enabled follow up of concerns identified in CDC's Vaccine Safety Datalink, studies from other countries, or by advisory committees
  - New tools: rapid queries, real time surveillance, studies with medical record review
- New internal processes and operating procedures
- Closer coordination with product offices
  - Rotavirus study: from regulatory question to regulatory action in < 3 years
- Fulfilled congressional mandate to strengthen postmarket safety's capabilities and role in product regulation

Four Strategic Priorities

1. Enhance detection of unexpected safety concerns using population based data sources
2. Create new routine surveillance options at licensure when additional safety data are desired
3. Improve safety surveillance of medical product exposures during pregnancy
4. Integrate hospital data sources to enable surveillance of intravenous and injectable products

A 3.3 Year Summary

- Created a new population-based surveillance system to help FDA identify, evaluate and manage medical product risks
- Strengthened the natural linkage between product approval and postlicensure safety monitoring within a single agency
- Balanced multiple mandates for scientific rigor, speed, breadth and transparency