Post-Marketing Surveillance Studies

Post-Marketing

The time period after regulatory approval and after the product can be purchased and used by the public

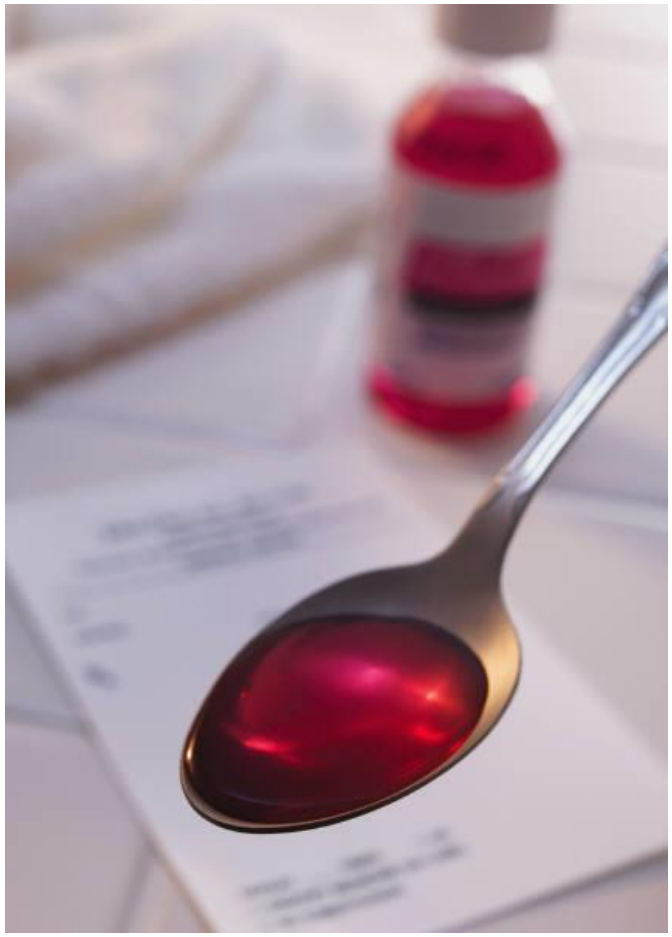
Surveillance

Non-experimental, observational framework under which information is collected

Study Methods

Data Collection, analytical and statistical methods used to transform the information into evidence to support safety and effectiveness

Post-Marketing Study Period



If these medical products are already available for physicians to prescribe and patients to use……..

Hasn't safety and effectiveness already been firmly established?

Safety and Effectiveness Already Established?

Experimental World

Yes

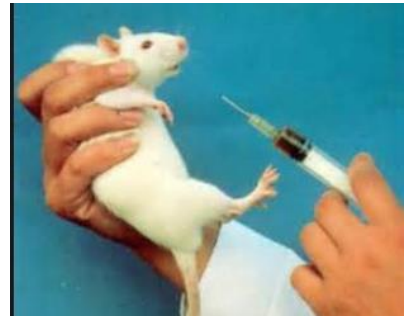
Real World

Not Quite Yet

Basic Research Compounds Screened

10,000

Preclinical Laboratory and Animal Test



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Pre Approval Human Investigation Clinical Trials (Experimental World)

Phase I — 20–100 subjects

Phase II — 100-500 subjects

Phase III — 1,000-10,000 subjects

< 5

1 New Drug Application Submitted for Approval

Pre Approval Human Investigation Clinical Trials (Experimental World)

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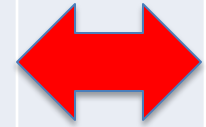
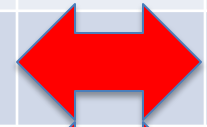
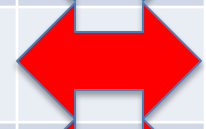
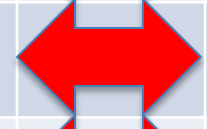
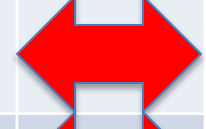
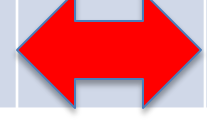
Approve

Disapprove

Experimental World		Real World
Patients selected by inclusion & exclusion criteria		Patients selected by physician and drug label
Trained investigators		No training required
Detailed study protocol		Drug label
Weekly, monthly visits		Visits much less frequent
Extensive labs and exams		Standard labs and exams
Dedicated staff		“Usual care” staff

Limitations of Premarketing Experimental Clinical Trials

- Small size of the study sample tested, often not adequately including special groups such as the elderly, children and women
- Narrow indications studied
- Exclusion of certain disease states
- Short duration of study
- Time period not reflective of a drug's potential chronic use

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Approval and Pre Marketing

Approved

Disapprove

- Manufacturing
- Packaging
- Drug Labeling
- Advertising
- Communications
- Education

Medical Product is Launched

- The product can now be prescribed and purchased by patients
- Phase IV clinical trials continue to experimentally evaluate safety and effectiveness for 2 – 3 years

Market Launch

Pre-Marketing Safety Data

Post-marketing Period

After market launch, the post-marketing surveillance season officially opens, and only ends if the product is removed from the market.

Public Health Surveillance Systems

Surveillance Systems

S.P.Y.
Intelligence
Services

Drones

Security Cameras

Baby Monitors

What do all surveillance systems have in common?

- Promote safety and prevent harm
- Collect information in an unobtrusive manner
- Monitoring is continuous and "silent"
- Real world activities are undisturbed
- Monitoring should not impact outcome
- Systems detect events and provide signals and alerts for potentially harmful, unsafe and suspicious activity

Public Health Surveillance

"The systematic collection, consolidation, analysis and dissemination of data in public health practice."

(Langmuir, 1963)

"The ongoing systematic collection, analysis, and interpretation of outcome-specific data for use in the planning, implementation, and evaluation of public health practice."

(Thacker, 2000)

WHO Global Alert and Response

Systematically gathers official reports and rumors of suspected disease outbreaks from

- Ministries of health
- National institutes of public health
- WHO Regional/Country offices
- Civilian and military laboratories
- Academic institutions
- Nongovernmental organizations

Epidemic Intelligence

Systematic Event Detection

- WHO global epidemic intelligence focuses on communicable diseases such as haemorrhagic fevers, cholera, meningitis, and encephalitis
- Also identifies related conditions such as food and water safety, and chemical events

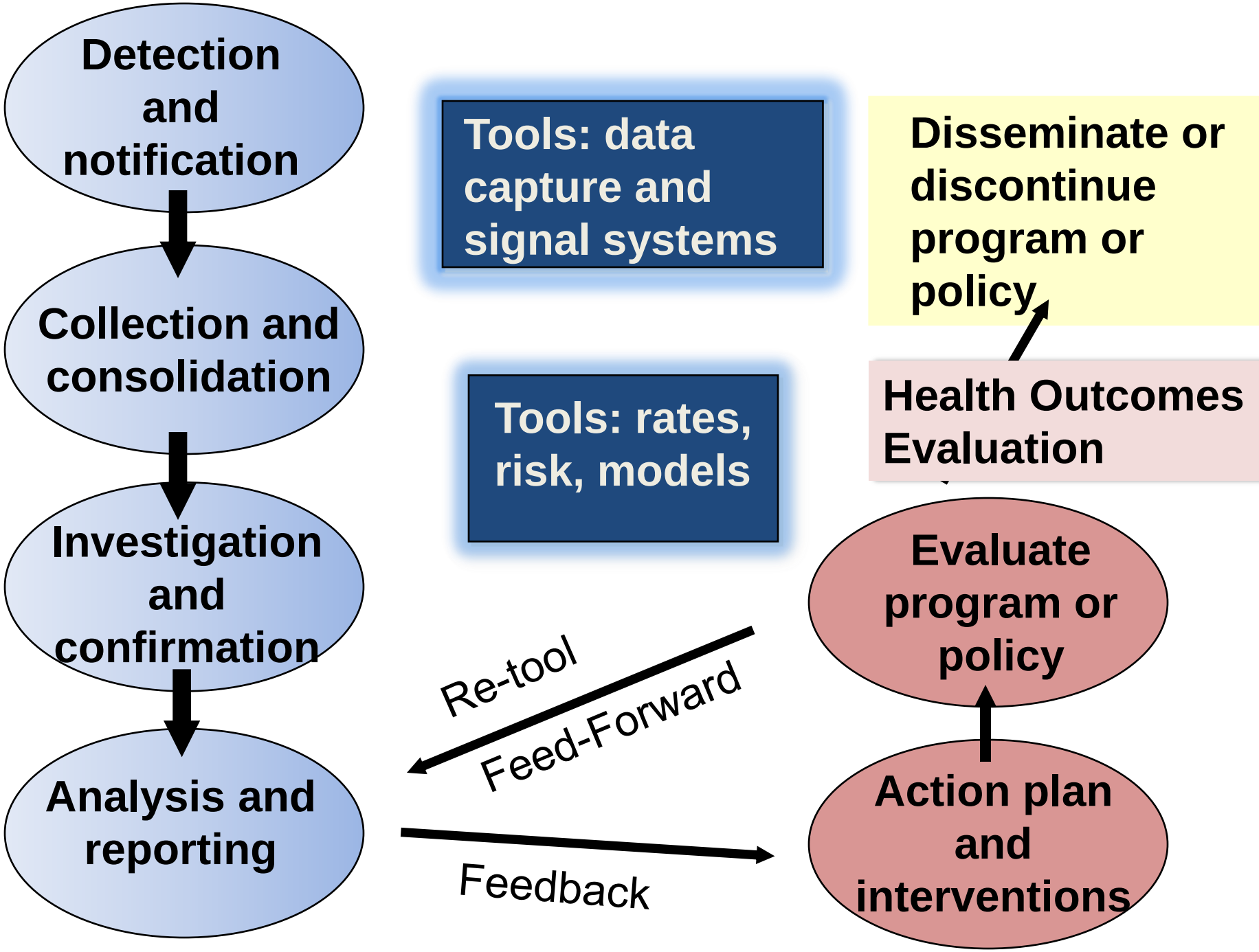
Public Health Surveillance System

"A public health surveillance system is defined as encompassing everything that supports the activity of collecting and monitoring disease data, including policies, laws, people, partners, information systems, processes, and resources at the local, state, and national levels."

Centers for Disease Control and Prevention

National Notifiable Disease Surveillance System

Fact Sheet


Detection and notification
Collection and consolidation
Investigation and confirmation
Analysis and reporting
Tools: data capture and signal systems
Tools: rates, risk, models
Disseminate or discontinue program or policy
Health Outcomes Evaluation
Evaluate program or policy
Action plan and interventions
Re-tool
Feed-Forward
Feedback

Passive Surveillance

- Routine reporting of the cases of diseases reaching health care facilities for treatment or service.
- No special effort is made to find unsuspected disease or adverse incidents.

Ref: CDC NNDSSFact Sheet

Passive Surveillance Advantages

- Relies on health professionals, patients or the manufacturer to voluntarily submit reports of disease or suspected adverse events associated with a medical product.
- No solicitation, simpler, less expensive, does not limit the target population
- Because of the broad pool of reporters, it offers potential for detecting rare events

Passive Surveillance Disadvantages

- Variability in reporting standards
- Reporter bias
- Significant under-reporting of events
- Reported events could be manifestations of the underlying disease under study
- Analytically difficult to separate the potential signal from the background noise

National Notifiable Diseases Surveillance System

Monitoring the Occurrence and Spread of Diseases

Effective public health surveillance begins at the local- and state-health department levels.

http://wwwn.cdc.gov/nndss/

TABLE I. Provisional cases of infrequently reported notifiable diseases (<1,000 cases reported during the preceding year), United States, week ending July 20, 2013 (WEEK 29)*

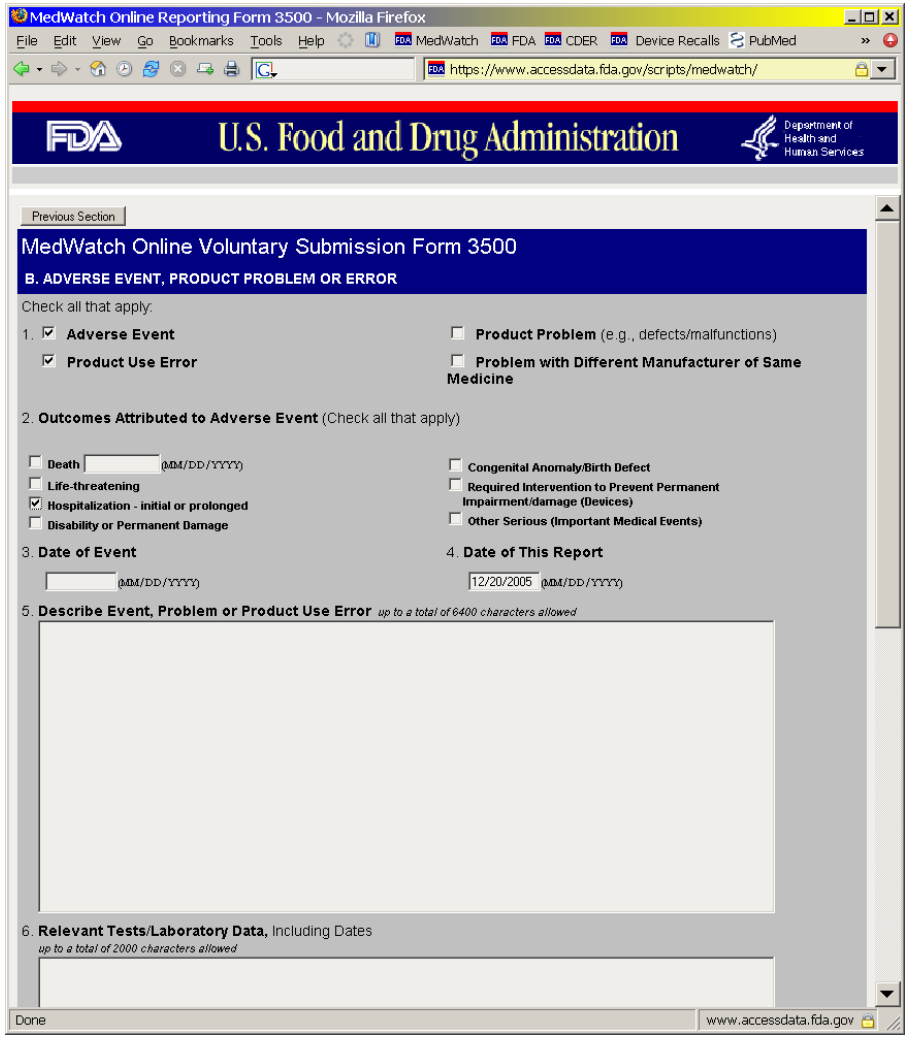
Disease	Current week	Cum 2013	5-year weekly average†	Total cases reported for previous years				
				2012	2011	2010	2009	2008
Anthrax	-	-	-	-	1	-	1	-
Arboviral diseases §, ¶ :								
California serogroup virus disease	-	3	5	81	137	75	55	62
Eastern equine encephalitis virus disease	-	2	0	15	4	10	4	4
Powassan virus disease	-	1	0	7	16	8	6	2
St. Louis encephalitis virus disease	-	-	0	3	6	10	12	13
Western equine encephalitis virus disease	-	-	-	-	-	-	-	-
Babesiosis	22	126	35	916	1,128	NN	NN	NN
Botulism, total	1	72	2	168	153	112	118	145
foodborne	-	2	0	27	24	7	10	17
infant	-	60	2	123	97	80	83	109
other(wound & unspecified)	1	10	0	18	32	25	25	19
Brucellosis	-	34	2	115	79	115	115	80
Chancroid	2	9	0	15	8	24	28	25

- The CDC NNDSS provides statistics in relatively, real time by local, state and national jurisdictions on any reportable disease.

The FDA Safety Information and Adverse Event Reporting Program

"Your FDA gateway for clinically important safety information and reporting serious problems with human medical products"

http://www.fda.gov/Safety/MedWatch/default.htm/



- Age, sex, weight
- Adverse events, use error, defects or malfunction
- Outcomes – death, life-threatening, hospitalization, disability, congenital anomaly, etc.
- Free text – problem description, labs, clinical history, comorbid diseases and other risk factors

Active Surveillance

- Targeted search for cases in the community mainly through case tracking, registries, structured forms and surveys.
- Includes the purposeful gathering of information from institutions and healthcare providers.

Active Surveillance Advantages

- Regular periodic collection of case reports (of drug events) from health care providers or facilities
- Links the disease or adverse event status of all persons in a defined population to their clinical outcomes minimizing under-reporting
- Allows collection on more complete data

Active Surveillance Disadvantages

- May be very expensive and difficult to implement
- Due to the comparatively small number of participants, may lack ability to detect very rare events or deaths
- Difficulty obtaining information from both in-patient and out-patient settings
- Developing a system that is timely, practical and efficient

Influenza Active Surveillance

Web-Site Resources

CDC Surveillance Resource Center

http://www.cdc.gov/surveillancepractice/index.html

FDA MedWatch

http://www.fda.gov/Safety/MedWatch/default.htm

FDA Sentinel Initiative

http://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm

Mini-Sentinel

http://www.minisentinel.org/

Visit each site and the associated links on the home pages.