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Supporting Drug Safety with PharmaPendium and advanced FAERS search functionality

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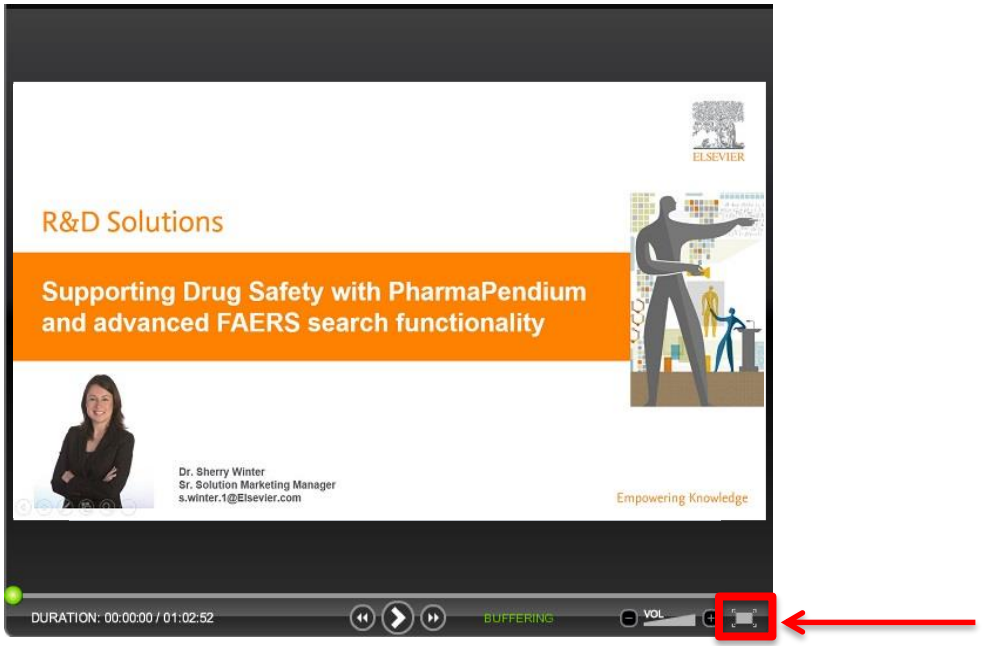
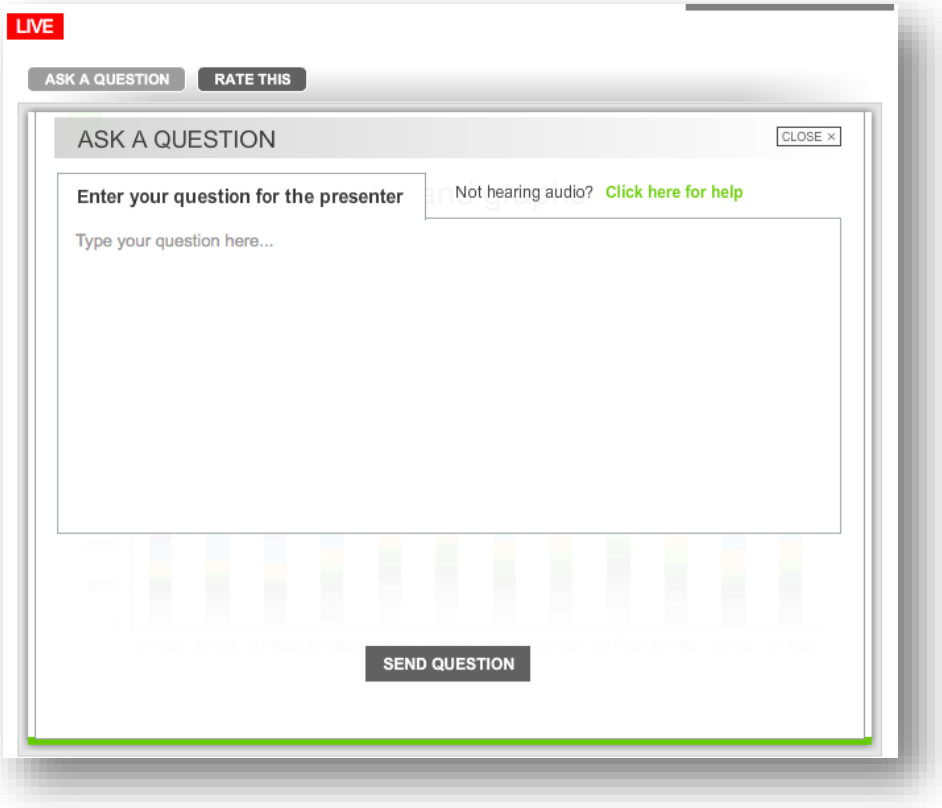
Empowering Knowledge

We suggest viewing the presentation in full screen



Questions?

- You are welcome to submit questions by using the “Ask a Question” feature on your screen.
- As many questions as possible will be answered after the webinar.
- Slides and the recording will be sent to you following the webinar and are also available in the PharmaPendium Help section

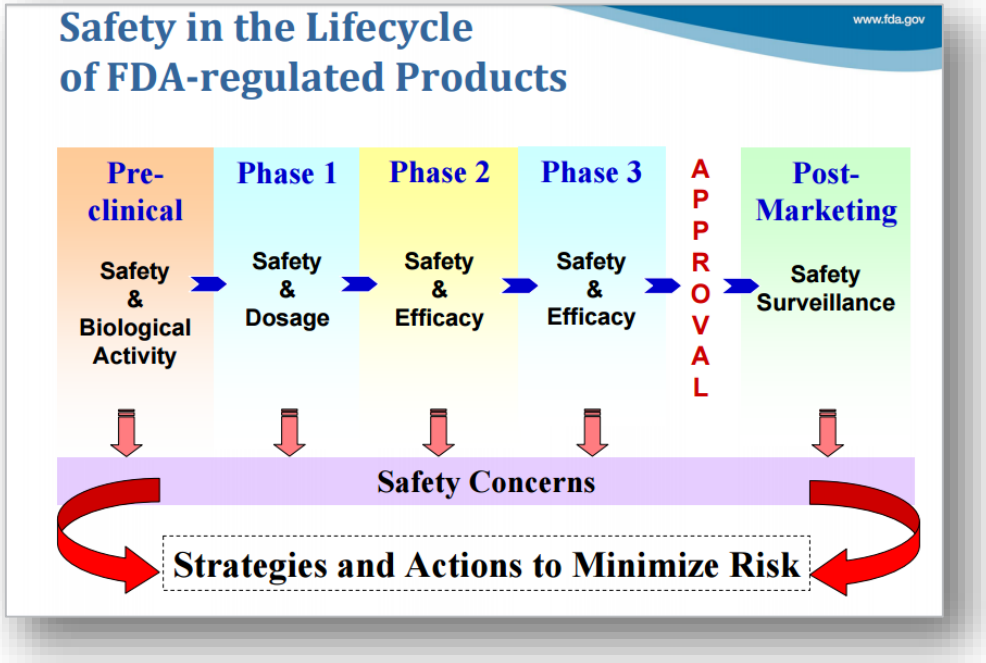


Agenda

- Impact of Drug Safety on patient safety and drug development
- Brief PharmaPendium overview
- Sources of safety information in PharmaPendium
- Different ways to find safety information in PharmaPendium (with examples)
  - Extracted drug safety information
  - Drug-drug interactions (DDIRC and MET)
  - Post-market safety information (FAERS search)

Drug safety is an ongoing priority

Understanding potential safety concerns begins with preclinical/ toxicology assessments and continues through to post-market safety

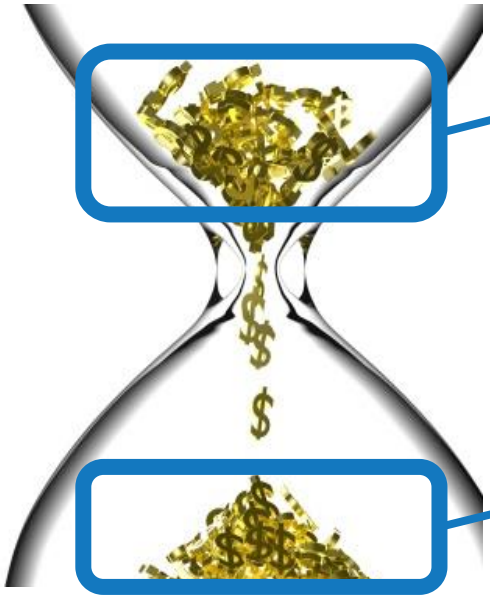


http://www.fda.gov/downloads/AboutFDA/WorkingatFDA/FellowshipInternshipGraduateFacultyPrograms/PharmacyStudentExperientialProgramCDER/UCM340626.pdf

Types of drug safety information we will focus on

- Comparative preclinical, clinical and post-market safety information found in Drug Approval documents and literature
- Information to identify and assess the potential impact of drug-drug interactions
- Post-market safety information the FDA Adverse Event Reporting system

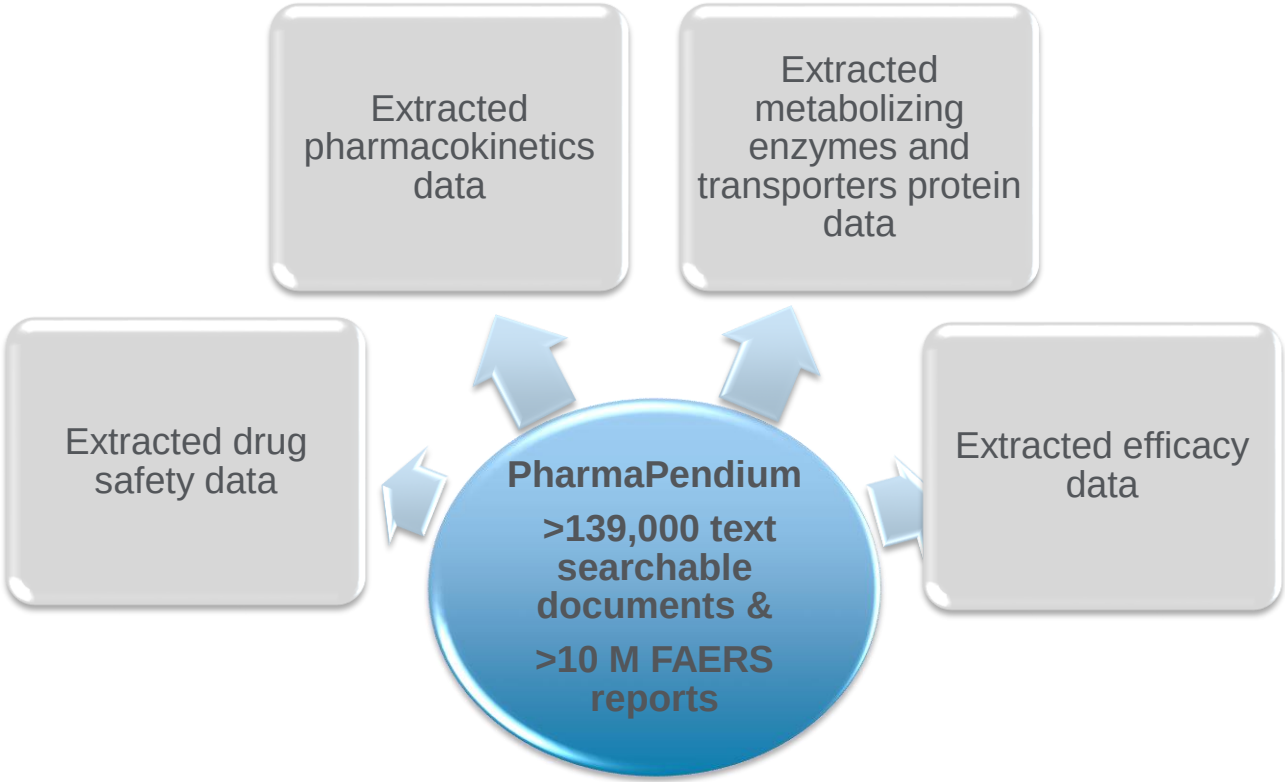
Critical decision-support for Drug Development



- ✓ Leverage past drug approvals to inform bottleneck issues
- ✓ Design studies that provide the most meaningful data
- ✓ Reduce unnecessary preclinical and clinical costs by comparing your drug to successful ones
- ✓ Rapidly evaluate potential DDI risks

PharmaPendium

Integrated FDA/EMA Drug Approval Docs & extracted data



Content and value is continually growing

Source Documents

2.3M+
pages of FDA approval documents

215K+
pages of EMA approval documents

10.4M+
FDA AERS reports

690K+
Pages from FDA Advisory Committee Meetings

Extracted Data

4485
Drugs indexed & fully searchable

1.64M+
PK data lines

315K+
Metabolizing enzyme and transporter data lines

1.71M+
safety data lines

2.71M+
efficacy data lines

115K
activity data lines

Drug Approval Packages

Safety information can be found throughout Drug Approval packages

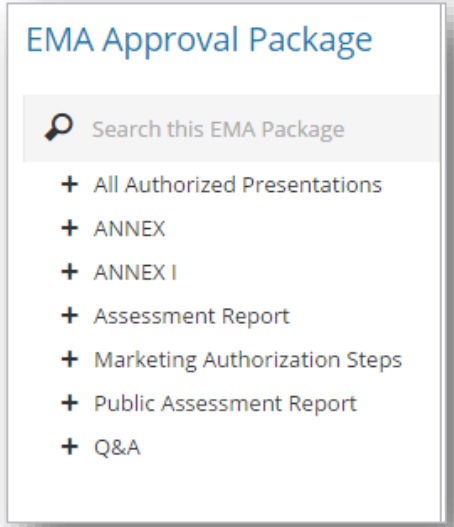
Main sections with safety information:

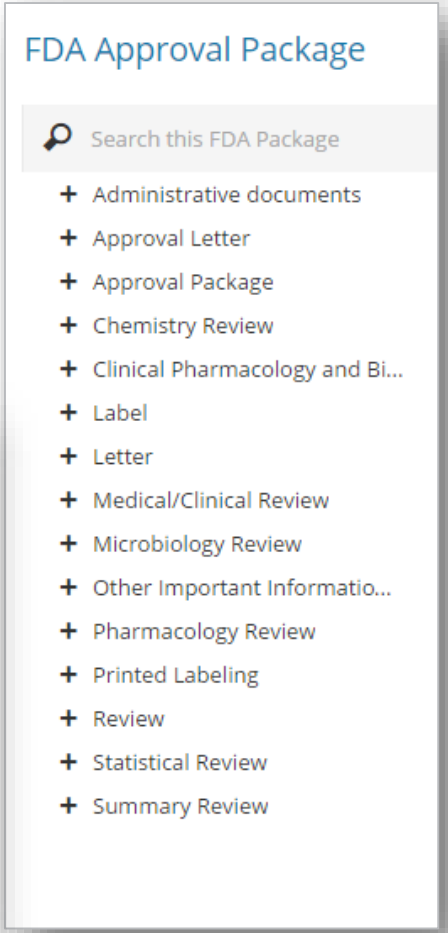
FDA

- Medical/Clinical Review
- Pharmacology Review
- Label/Printed Labeling

EMA

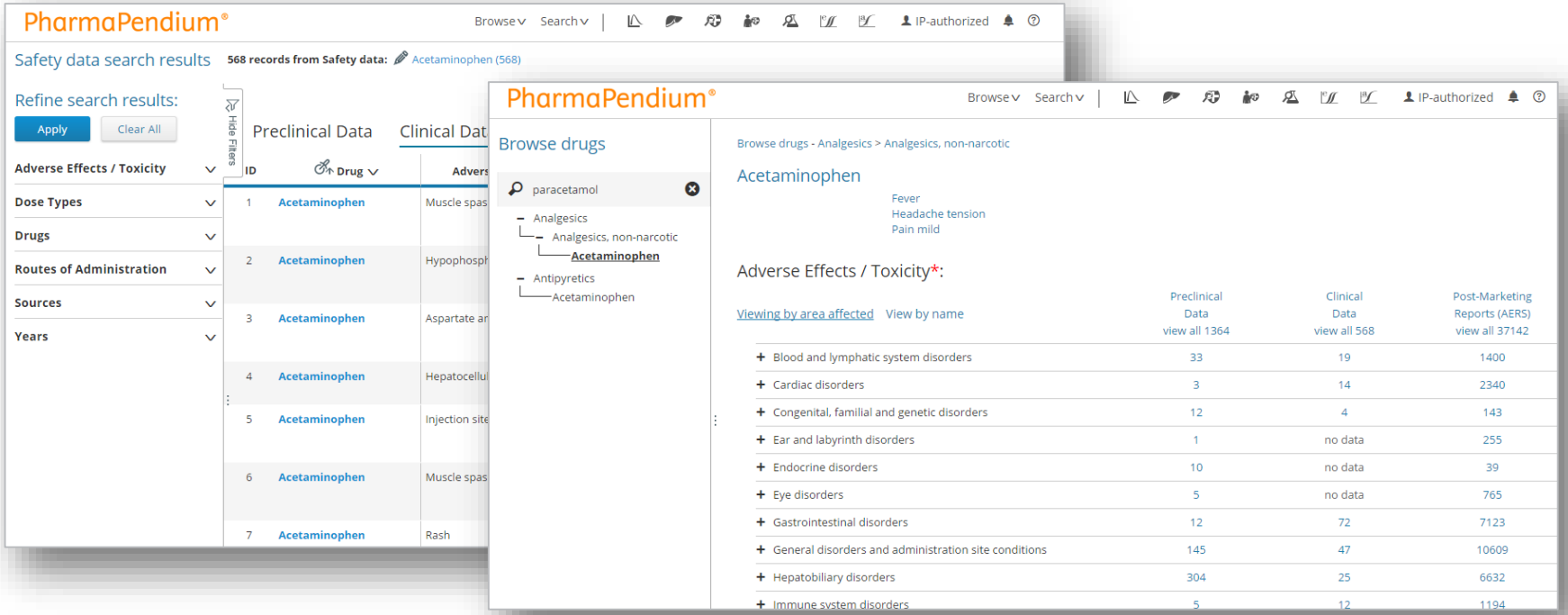
- Assessment Report
- Marketing Authorisation Steps
- ANNEX





Searching for safety information in PharmaPendium

- Extracted safety data, Text searchable data, FAERS reports



Search using a wide range of Drug Safety parameters

Adverse Events/Toxicity

AE taxonomy

- Normalized to MedDRA
- Unique translational view of AEs across preclinical, clinical and post-market

Species

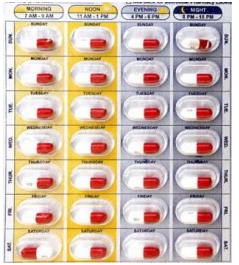
Includes:

- Human
- Vertebrates
  - Birds
  - Fish
  - Mammals

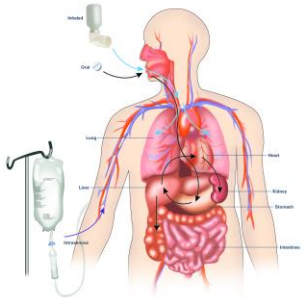
Dose, dose types

Includes:

- Extracted dose data
- Single/ repeated dose



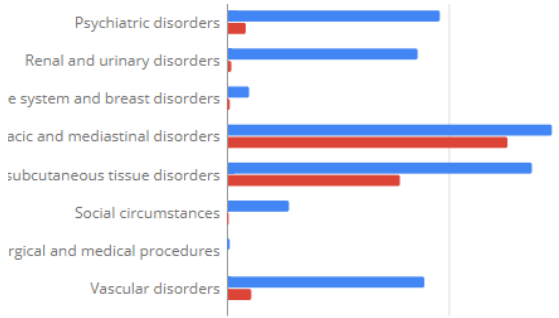
Route of administration



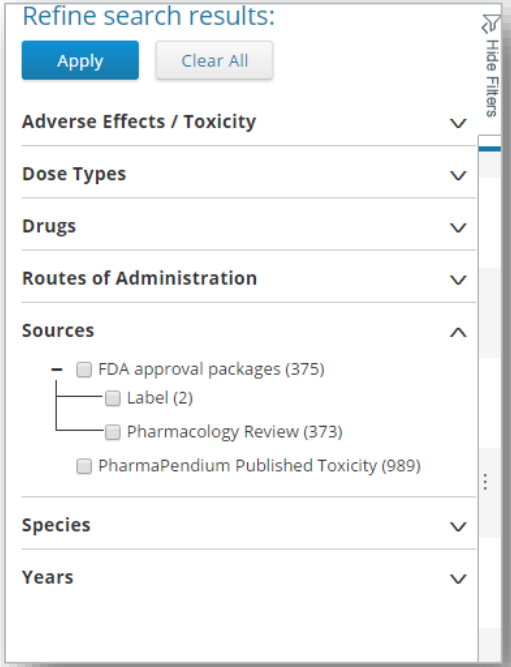
Post-market data – also searchable using the FAERS Search form

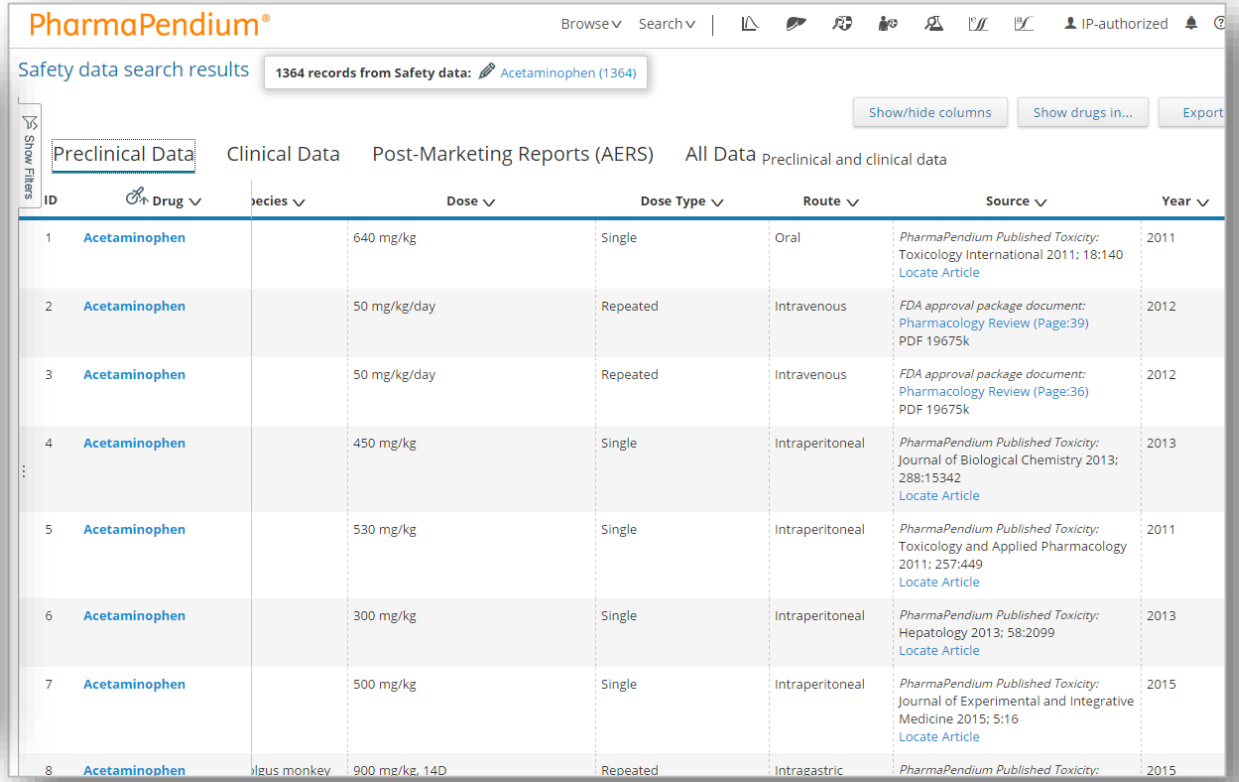
Includes:

- Drug role (primary, secondary, concomitant, interacting)
- Outcome (serious/non-serious)
- Age/gender
- Reporter occupation
- Route of administration
- Drug manufacturer

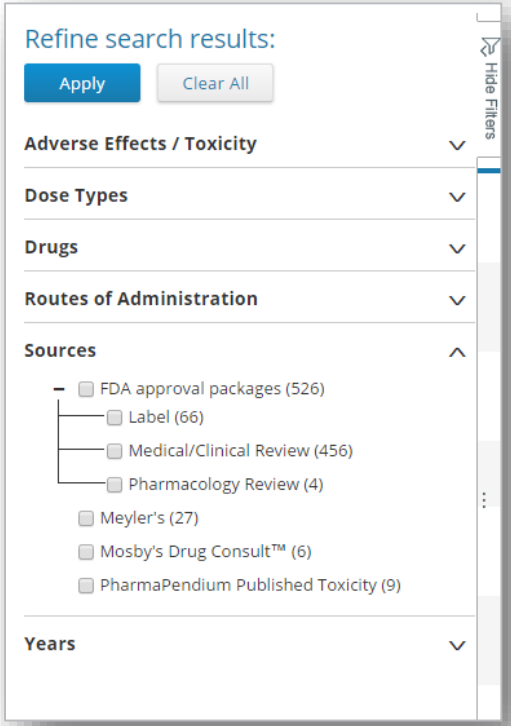


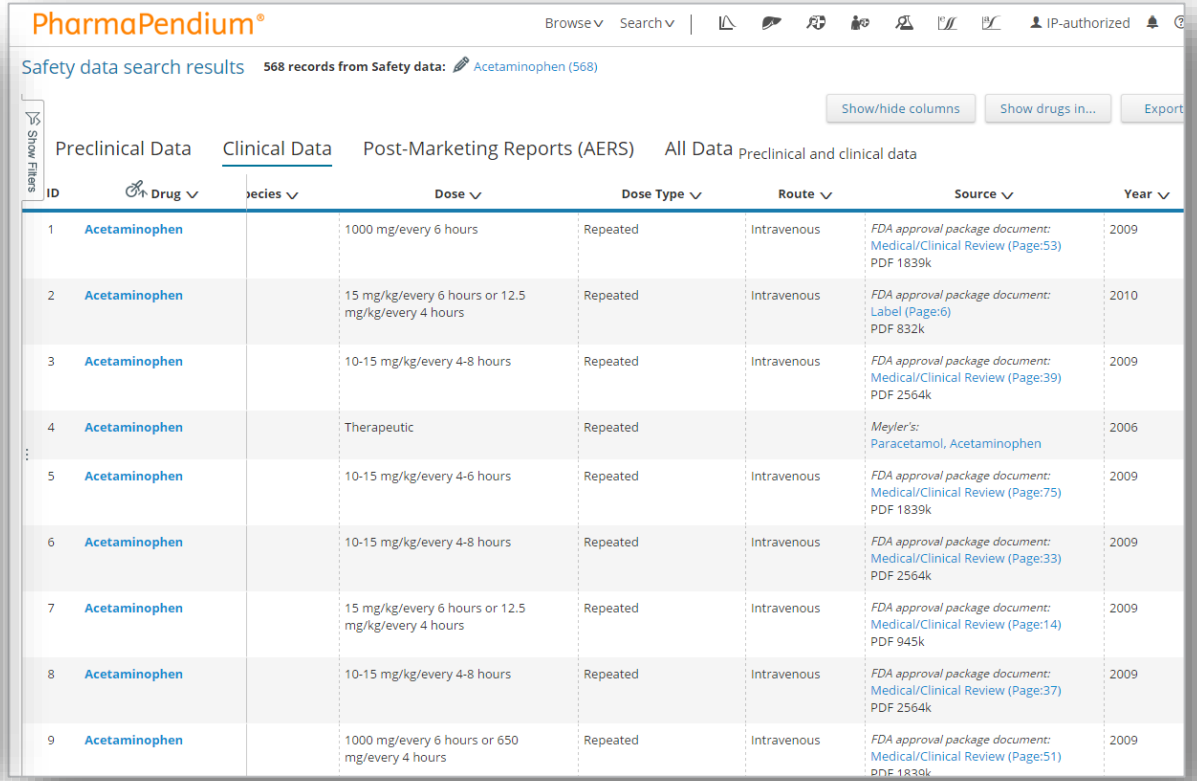
Sources of extracted preclinical safety data





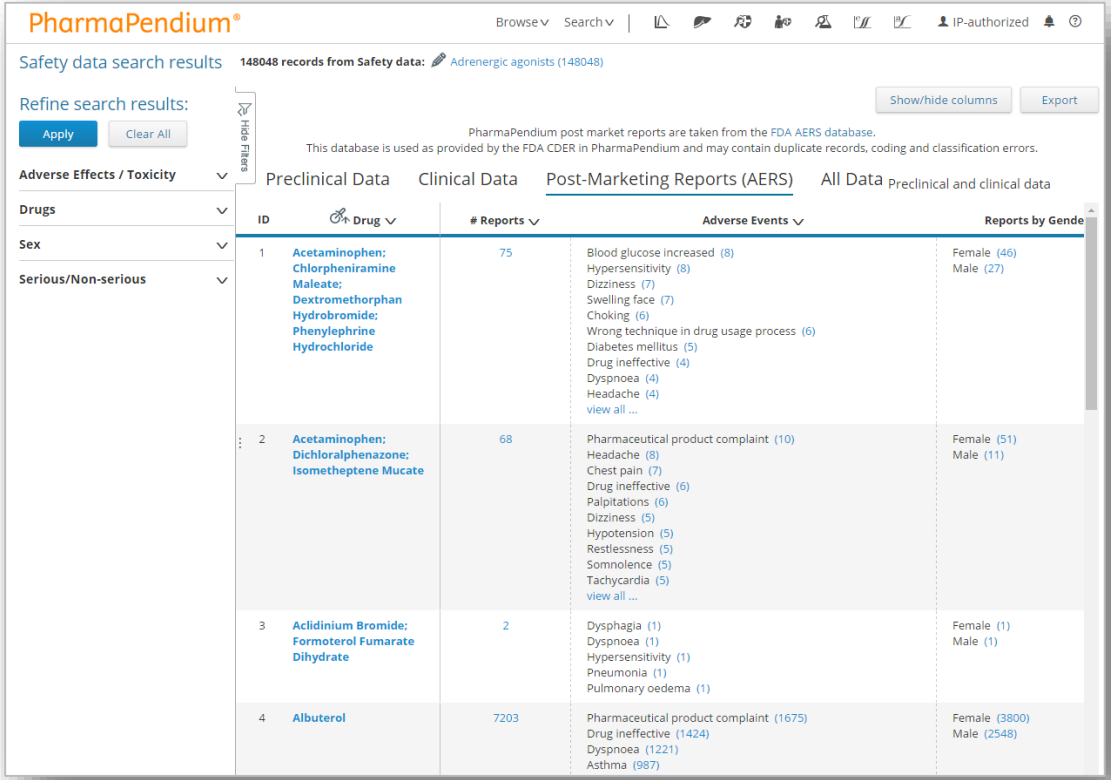
Sources of extracted clinical safety data



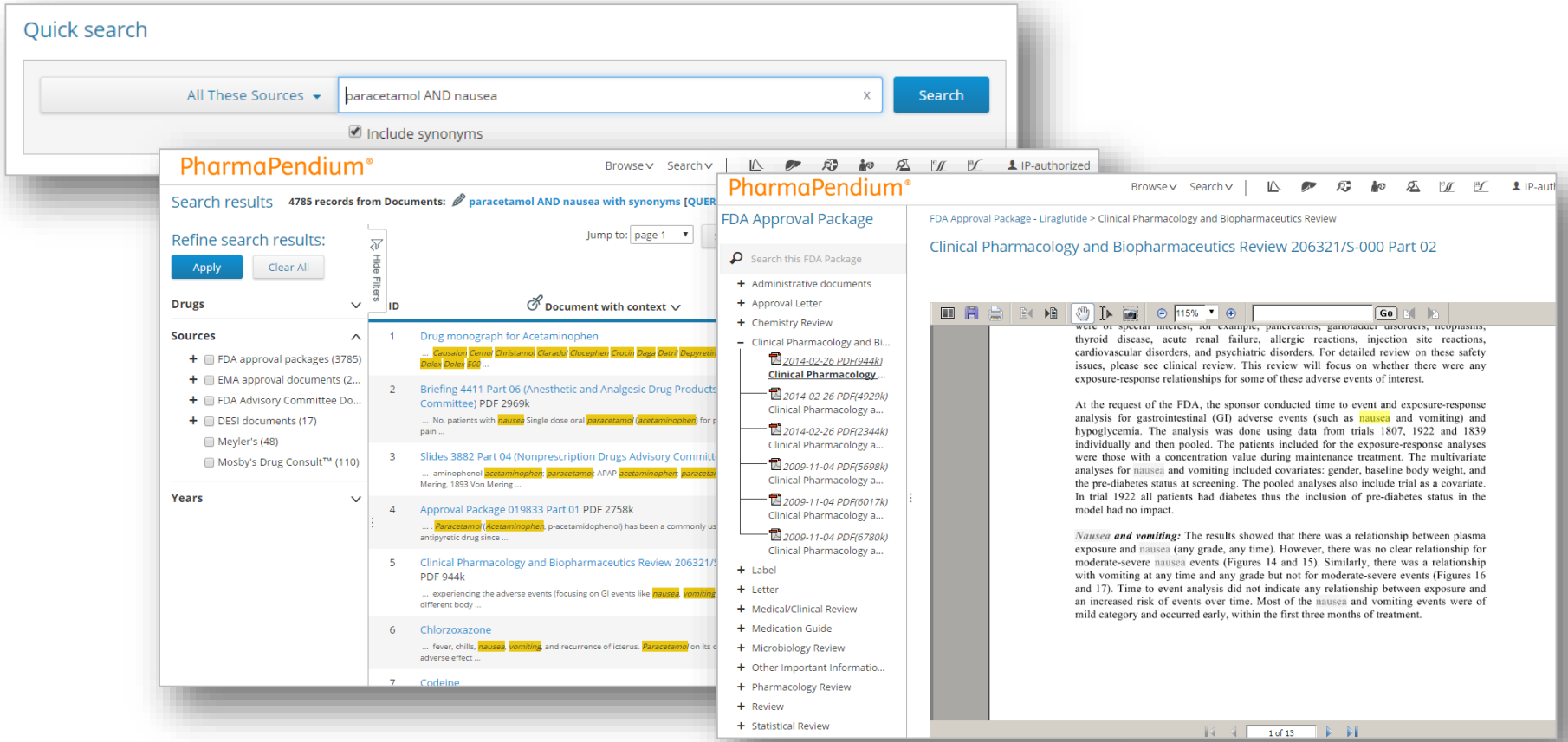


ID	Drug	Species	Dose	Dose Type	Route	Source	Year
1	Acetaminophen		1000 mg/every 6 hours	Repeated	Intravenous	*FDA approval package document:* Medical/Clinical Review (Page:53) PDF 1839k	2009
2	Acetaminophen		15 mg/kg/every 6 hours or 12.5 mg/kg/every 4 hours	Repeated	Intravenous	*FDA approval package document:* Label (Page:6) PDF 832k	2010
3	Acetaminophen		10-15 mg/kg/every 4-8 hours	Repeated	Intravenous	*FDA approval package document:* Medical/Clinical Review (Page:39) PDF 2564k	2009
4	Acetaminophen		Therapeutic	Repeated		*Meyler's:* Paracetamol, Acetaminophen	2006
5	Acetaminophen		10-15 mg/kg/every 4-6 hours	Repeated	Intravenous	*FDA approval package document:* Medical/Clinical Review (Page:75) PDF 1839k	2009
6	Acetaminophen		10-15 mg/kg/every 4-8 hours	Repeated	Intravenous	*FDA approval package document:* Medical/Clinical Review (Page:33) PDF 2564k	2009
7	Acetaminophen		15 mg/kg/every 6 hours or 12.5 mg/kg/every 4 hours	Repeated	Intravenous	*FDA approval package document:* Medical/Clinical Review (Page:14) PDF 945k	2009
8	Acetaminophen		10-15 mg/kg/every 4-8 hours	Repeated	Intravenous	*FDA approval package document:* Medical/Clinical Review (Page:37) PDF 2564k	2009
9	Acetaminophen		1000 mg/every 6 hours or 650 mg/every 4 hours	Repeated	Intravenous	*FDA approval package document:* Medical/Clinical Review (Page:51) PDF 1839k	2009

Sources of extracted post-market safety data



Text-searchable safety information in PharmaPendium



Demo 1: Search extracted safety information

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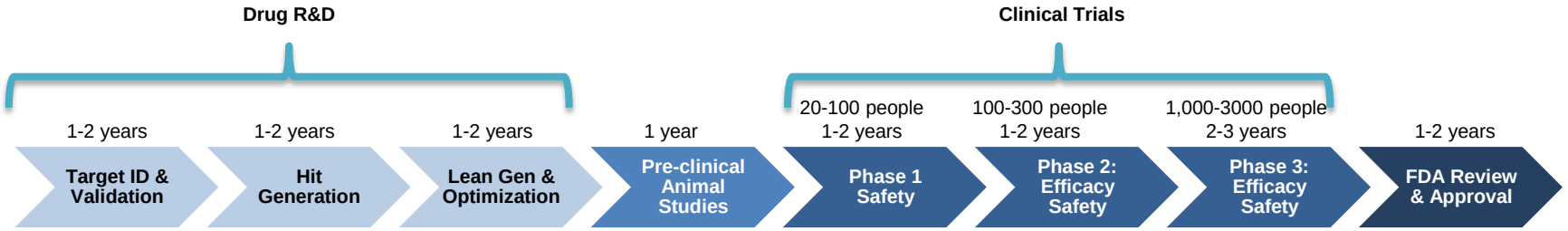
Empowering Knowledge

Accurate prediction of DDIs informs key decisions



For in-licensing, use DDIRC to:
- Determine if compound should be in-licensed
- Assess prioritization of projects/studies related to in-licensed drug

Optimize early drug candidate selection based on DDI risk

Prioritize clinical DDI studies

Identify unnecessary clinical DDI studies

Assess feasibility of combination therapy

Assess DDI Risk with unavoidable co-meds

Optimize clinical trial design (inclusion/exclusion criteria)

Assess effect of exposure increase to optimize dose selection

Depending on type of DDI (competitive/MBI inhibition or induction), better assess onset and duration of DDI effect

Recommend alternative drugs that may be co-administered to reduce DDI risk*

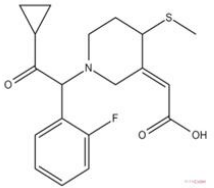
Recommend alternate doses for co-medications to reduce DDI risk*

* Including Phase 1, since for oncology indications, Phase 1 studies are done on patients, not healthy volunteers

Search using a wide range of MET parameters

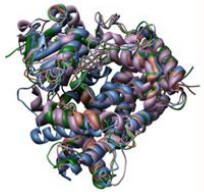
Metabolites

Created, when available

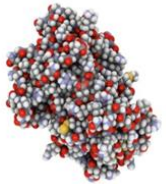


CYPs

Either involved in the metabolism or up/down regulated by the drug, quantitative and qualitative data

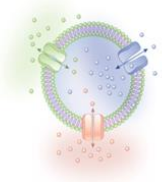


Phase 2 Enzymes



Transporters

And drug effects on transporters



In Vitro

***Dynamic* parameters** such as CLint (Intrinsic Clearance) and Km (Michaelis Constant), Vmax (Maximum rate of reaction)

DDI Studies

Ratio of AUC, Clearance, etc. in presence of another drug.

All with drug as: **Substrate, inducer or inhibitor**

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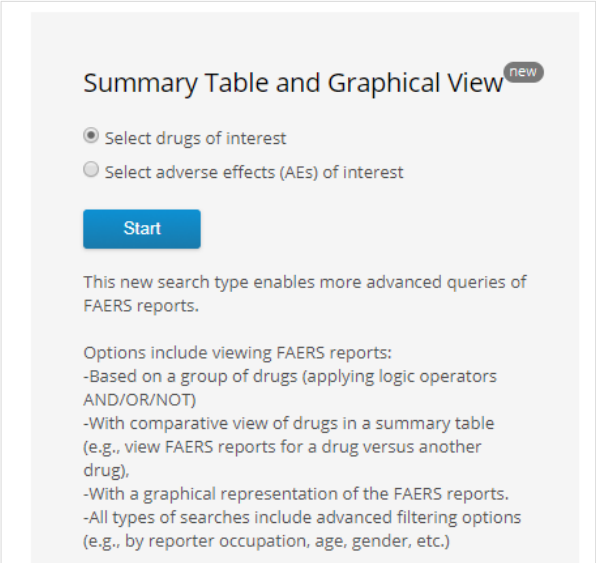
Demo 2 – predict DDIs (DDIRC and MET)

Empowering Knowledge

Spontaneous reporting databases

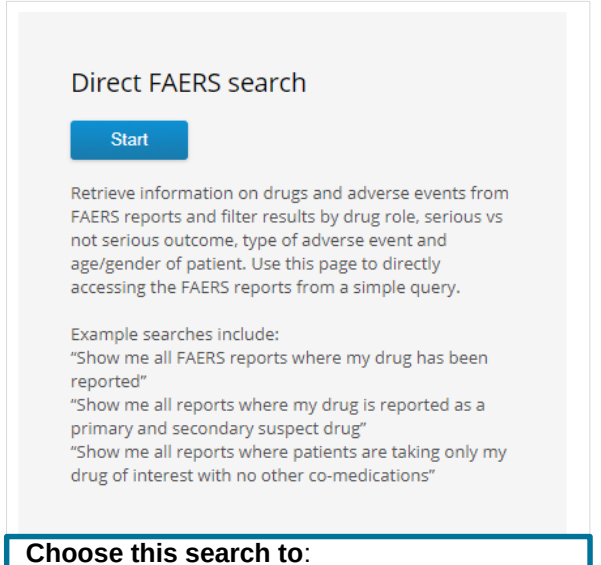
VigiBase	EudraVigilance	FAERS
Organization: The World Health Organization for International Drug Monitoring **Established:** 1968 **Number of records:** >14 million individual case safety reports (ICSR) from 110 participating countries. **Type of data:** ICSRs of post-marketing spontaneous serious and non-serious cases. Case reports from studies, clinical trials, special monitoring and literature are sometimes included. Data accessible only to authorized representatives of member countries.	**Organization:** European Medicines Agency **Established:** 2001 **Number of records:** >9.5 million adverse reaction reports referring to >6 million individual cases **Type of data:** ICSRs reported by national medicine authorities and MAH. The EMA publishes regular summaries of suspected adverse drug reactions, but national competent authorities are responsible for regular review and analysis of safety signals from the database.	**Organization:** The United States Food Drug Administration (FDA) **Established:** 1969 **Number of records:** >9 million reports **Type of data:** Contains information on adverse events and medication error reports submitted to the FDA by consumers, health practitioners and drug manufacturers.
VigiBase and **EudraVigilance** collect ICSRs that MAHs and Competent Authorities of member countries are **required** to submit upon notification of a possible adverse event. The adverse event may come to their attention through spontaneous reporting by consumers and healthcare professionals, mandatory reporting from clinical trials and structured post-marketing surveillance programs, medical literature, monitored internet sites, and more. ICSR refers to the format and content for the reporting. A valid ICSR should include at least one identifiable reporter, one single identifiable patient, at least one suspect adverse reaction and at least one suspect medicinal product.		**FAERS** includes mandatory reports of adverse events from drug manufacturers, distributors and other stakeholders as ICSRs. The database also includes voluntary reporting on adverse events or medication errors from healthcare professionals and consumers.

Perform comparative or direct FAERS searches



NEW – choose this search to:

- Compare and visualize AEs reported for a drug or group of drugs
- Build your own drug groups (e.g., with/without a drug, by role [primary vs secondary suspect], etc.)
- Apply filters (e.g., reporter occupation) to compare AEs reported for a drug/drug group



Choose this search to:

- Look for AEs reported for a drug, drug class or by indication and to access FAERS reports directly
- Search for reports of drugs in any role
- Filter for co-medications of interest
- Apply filters (e.g., seriousness of outcome, age and date) to narrow down results
- See details from reports in tabular form and export results for further analysis

FAERS searching lets you quickly compare safety data

- ✓ Compare the number of FAERS reports for a drug versus drug class
- ✓ View drugs reported as a primary or secondary suspect drug
- ✓ Look up FAERS reports related to a particular therapy where patients may be on multiple drugs, irrespective of the drugs' reported role
- ✓ Compare the adverse effect profile across drugs that belong to the same drug class
- ✓ Compare the adverse effect profile across demographic characteristics such as age and gender
- ✓ View reports where Drug A is reported but not Drug B
- ✓ Filter/segment the reports based on (e.g.,) who has filed the report or by route of administration

Demo 3: Leveraging FAERS to identify safety concerns

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Thank You!

Any Questions?

For more information:

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