Introduction to PharmaPendium

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Need to know

Webinar control panel:
• ‘Ask a question’ for questions and comments
• Option for full screen view
• Q&A at the end
Agenda

• PharmaPendium overview
• Focus on:
  – Content
  – Taxonomies
• Text searching vs extracted information
• Overview of modules
• Examples – leveraging information in PharmaPendium
  – Drug safety
  – FAERS
  – PK
A Critical Decision-Support Solution for Drug Development
Assess drug safety and efficacy, prioritize drug candidates, mitigate risk

- 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

PharmaPendium
PharmaPendium integrates FDA/EMA Drug Approval Documents and extracted data for seamless searching across different types of information.

- Extracted pharmacokinetics data
- Extracted metabolizing enzymes and transporters protein data
- Extracted drug safety data
- Extracted efficacy data

PharmaPendium >139,000 text searchable documents & >10 M FAERS reports
Our Process and Industry's challenge

Made regulatory documents easily accessible

Inputs
- FDA Drug Approval Documents back to 1938
- EMA Drug Approval Documents back to 1995
- FDA AERS
- FDA Advisory Committee Meeting Reports
- Journal Articles

Transformation
- Make documents text searchable
- Define taxonomy
- Develop databases structure
- Manual review by panel of experts
- Extract observations on Safety, Pharmacokinetics, Efficacy and Metabolizing enzymes and Transporters

Outputs
- Searchable, indexed database all linked back to original documents
- All extracted information searchable across drug, class and chemical structure
- Data ready to be exported into analytical modeling tools
Leverage insights from PharmaPendium to make more impactful competitive drug safety and efficacy decisions

Drug Safety and ME&T Modules
FAERS Searching

PK and ME&T Modules

Efficacy Module

Must prove better performance in one or more of these areas

Safety
Deliverability
Efficacy
PharmaPendium 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

Content as of October 2017
PharmaPendium taxonomies

• Adverse effects taxonomy
  ▪ Taxonomy contains MedDRA preferred terms and synonyms linked to MedDRA preferred terms

• Targets taxonomy
  ▪ Target information and the relationship between targets and drugs comes from xPharm, drug labels and FDA Approval Packages

• Endpoint taxonomy
  ▪ Developed in-house

• Indications taxonomy
  ▪ Based on MedDRA with additional indications from Mosby’s Medical Dictionary

• Drug names
  ▪ FDA generic drug names are the main PharmaPendium drug name
  ▪ European drug names are taken primarily from Meyler’s
  ▪ Synonyms are linked to the main drug name

• Excerpted PK, MET and efficacy data based on defined thesauri/parameters
Our users report that PharmaPendium supports confident decision-making and informs product positioning.

Why is that critical?

72% of surveyed research organizations agree that PharmaPendium provides important insights that impact the success of a project.
PharmaPendium helps you understand the benchmarks for success

**Drug Safety**
- Can I cite a previously-run experiment from a similar drug?
- Has this problem occurred before? If so, how was it successfully argued?
- Do similar drugs have post-market safety concerns that could inform my risk mitigation strategy?

**Therapeutic Index**
- What is the maximum amount of drug in the blood plasma (Cmax)?
- How long does it stay there (T1/2)? At what rate does it clear out (CL)?

**DDIs**
- Do these parameters change in the presence of other drugs, or based on disease state of the patient?
- What role does CYP3A4 play in drug metabolism in this drug class?
- Do post-market AE reports suggest a potential DDI?

**Drug Efficacy**
- What is the best patient (sub)population to test?
- Which primary endpoints were used during Phase III clinical trials for similar drugs?

**Competitive Intel**
- What post-market adverse events have been seen for competitor drugs?
- What efficacy and safety benchmarks need to be met to compete?
How to search? Text search vs. extracted data

Text search

Quick search
How to search? Text search vs. extracted data

Extracted data search
Search extracted data in Safety, PK, Efficacy and ME&T modules or perform dedicated FAERS searches.
Search using a wide range of Drug Safety parameters

- Unprecedented access to >10M FAERS reports and more than 1.7 million lines of safety data extracted from FDA and EMA Drug Approval documents for 4,485 drugs

Extracted information lets you limit or filter searches by specific parameters including:

### 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
Example: Leverage comparative information in PharmaPendium to increase the likelihood of clinical trial/regulatory success
Challenge: Specific Adverse Event is seen in clinical trials

- Has this problem occurred before? If so, how was it successfully argued?
- What new secondary experiments are needed prior to submission, if any? How were these experiments designed?
- Can I cite a previously-run experiment from a similar drug?
- How does the risk of seeing this adverse event clinically compare with other competitors?
Example – Somnolence as an AE for opioid receptor agonists

Somnolence is observed in clinical trials as an adverse event for a k-opioid receptor agonist. Examine comparative information in PharmaPendium to inform further clinical studies and maximize the success of a regulatory submission

1. Browse Targets for opioid receptor/kappa
View safety data for drugs with same target

2. View Drug Safety Data
Filter results for specific AE of interest

3. Filter results for relevant AEs to see a list of drugs where these effects have been reported
Further filter down to find comparative data for similar, marketed drugs

3. Look more closely at drug(s) with similar chemical structure (e.g., Buprenorphine)
Reference: Table 64. Number (%) of Subjects with Adverse Events Leading to Study Drug Discontinuation in ≥1% of Subjects by Treatment Group During the Double-Blind Period of Enriched, Fixed Duration, Chronic Pain Studies (Group A2B), pg. 201 of ISS

Dose Reductions Due to Adverse Events

The most common reasons by system organ class for dose reductions during the open-label extension period of the chronic pain studies were gastrointestinal disorders (2.0%) and nervous system disorders (1.8%). The most common reasons for dose reduction by preferred term were: nausea (1.6%); vomiting (0.4%); application site erythema (0.4%); fatigue (0.4%); dizziness (0.8%) and somnolence (0.8%). In the enriched, fixed-duration studies (Group A2B), only study BDP3024 allowed dose reduction. In this study during the open-label run-in period, 2/1024 (0.2%) subjects experienced AEs that led to dose reduction. In the double-blind period, 6/256 (2.3%) STDS-treated subjects and 2/283 (0.7%) placebo-treated subjects experienced AEs that led to dose-reduction.

7.3.4 Significant Adverse Events

Discussed in section 7.3.2
Find additional information to support successful clinical trial design and regulatory submissions

Questions to consider: what placebo was used in these clinical trials? What patient populations were used? What arguments were used with FDA/EMA to demonstrate positive risk/benefit?

e.g., Efficacy data provides information on dosage, comparative groups and study populations

e.g., FDA Approval Package includes Risk Evaluation and Mitigation Strategy information
Search extracted data in Safety, PK, Efficacy and ME&T modules or perform dedicated FAERS searches
Example:

How can we see if the reporter occupation affects the number of FAERS reports? (start search by selecting drug of interest)
How do AEs compare when different filters are applied?
- Select drug of interest

Summary Table and Graphical View
- Select drugs of interest
- Select adverse events (AEs) of interest

Options include viewing FAERS reports:
- Based on a group of drugs (applying logic operators AND/OR/NOT)
- With comparative view of drugs in a summary table (e.g., view FAERS reports for a drug versus another drug),
- With a graphical representation of the FAERS reports.
- All types of searches include advanced filtering options (e.g., by reporter occupation, age, gender, etc.)

Direct FAERS search
- Start

Retrieve information on drugs and adverse events from FAERS reports and filter results by drug role, serious vs not serious outcome, type of adverse event and age/gender of patient. Use this page to directly accessing the FAERS reports from a simple query.

Example searches include:
- “Show me all FAERS reports where my drug has been reported”
- “Show me all reports where my drug is reported as a primary and secondary suspect drug”
- “Show me all reports where patients are taking only my drug of interest with no other co-medications”

Watch tutorial for a quick tour!
To add drugs or drug groups to compare, click on ‘Add drugs’
Search for Accutane (note that this drug synonym/brand name is mapped to the preferred term Isotretinoin)

Studies show that there is signal distortion for Accutane due to disproportionate reporting by attorneys.

PharmaPendium FAERS search lets you quickly see this disproportionate reporting.
Apply filters to compare between FAERS reports by health professionals vs lawyers
There is a clear spike in the number of gastrointestinal disorders reported by lawyers (Filter #2).
It is important to understand and validate signals.

There is clearly higher reporting for GI AEs by lawyers compared to healthcare professionals.

Filter 0 = unfiltered data
Filter 1 = healthcare professionals
Filter 2 = lawyers
Search extracted data in Safety, PK, Efficacy and ME&T modules. Or perform dedicated FAERS searches.
Examine PK parameters that determine therapeutic window
Search using a wide range of PK parameters

- Unprecedented access to more than 1.6 million lines of preclinical and clinical exposure data extracted from FDA packages (current & historic) and EMA documents for 4,485 drugs

Extracted information lets you limit search to specific parameters including:

**Absorption**
Includes:
- % Absorbed
- Bioavailability
- Concentrations
- Fraction absorbed
- Time values

**Binding**
Includes:
- Cell binding
- Protein binding

**Biotransformation**
Includes:
- Enantiomeric ratio
- Metabolic ratio
- Metabolic stability
- Metabolic transformation

**Distribution**
Includes:
- Accumulation
- AUC
- Permeation
- Steady state
- Time value
- Tissue distribution
- Volume of distribution

**Elimination**
Includes:
- Clearance
- Excretion values
- Half life
- Rate constants
- Time

**Species**
Includes:
- Human
- Vertebrates
- Birds
- Fish
- Mammals
Example

• Have ethnic variations that could affect dosage been observed for drugs similar to mine?
• How was this communicated to the regulatory body?
• What follow up studies were needed?
Have ethnic variations that could affect dosage been observed? - Select the drug similar to the investigational drug
Have ethnic variations that could affect dosage been observed?
- Select the parameters to investigate
Have ethnic variations that could affect dosage been observed? - Compare study groups – are there any differences?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Species</th>
<th>Study Group</th>
<th>Dose</th>
<th>Route</th>
<th>Parameter</th>
<th>Value</th>
<th>Units</th>
<th>Parameter Normalized Value</th>
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<td>advanced solid tumors</td>
<td>0.75 mg/kg</td>
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<td>Cmax</td>
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<td>(119 to 119)</td>
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<td>Intravenous</td>
<td>Cmax</td>
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<td>Intravenous</td>
<td>Cmax</td>
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<td>(52.3 to 52.3)</td>
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</tr>
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<td>metastatic colorectal ca</td>
<td>2.5 mg/kg</td>
<td>Intravenous</td>
<td>Cmax</td>
<td>52.3</td>
<td>(52.3 to 52.3)</td>
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<td>Cmax</td>
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<td>57</td>
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<td>ug/mL</td>
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<td>Cmax</td>
<td>213</td>
<td>(154 to 272)</td>
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</tbody>
</table>
Have ethnic variations that could affect dosage been observed? - Compare study groups – are there any differences?

<table>
<thead>
<tr>
<th>Value</th>
<th>Units normalized Value (only standard units)</th>
<th>Only std.</th>
<th>SD</th>
<th>I</th>
<th>Concomitant</th>
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</thead>
</table>
| 34 | ug/mL | 13.0 to 20.0 | ug/mL | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 28 | 24 to 31 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 34 | 26 to 40 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 50 | 40 to 53 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 55 | 55 to 65 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 60 | 54 to 70 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 62.5 | 58.3 to 66.3 | ug/mL | 22.6 | week 17 | | FDA approval package document: Scientific Discussion paper 19-059 | https://www.srmapharmac.com/
| 62.5 | 58.3 to 66.3 | ug/mL | week 17 | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 65.1 | 55.1 to 75.1 | ug/mL | week 26 | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 6 | 8 to 10 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 6.3 | 8.3 to 9 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 8 | 8 to 10 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 6 | 8 to 10 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 52.3 | 45.6 to 59.0 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 52.3 | 45.6 to 59.0 | ug/mL | week 35 | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 44 | 44 to 44 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 41 | 38 to 42 | ug/mL | | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
| 43 | 38 to 42 | ug/mL | week 44 | | | FDA approval package document: Clinical Pharmacology and Bioavailability | https://www.srmapharmac.com/
Go directly to the source to see context – you can also search for specific terms to quickly find relevant information.
Go directly to the source to see context
study report will provide summary analyses of pharmacokinetic and safety information and primary data used to generate the analyses in an electronic, SAS-compatible dataset. The final protocol will be submitted by August 31, 2007. Patient accrual will begin by December 31, 2007, and the study will be completed (last PK sample for last enrolled patient) by April 1, 2009. The final study report will be submitted by August 30, 2009.

10. To submit a final study report for study 20040192 entitled, “A Phase 1 Clinical Study of ABX-EGF (Panitumumab) Evaluation of the Safety and PK of ABX-EGF in Japanese Subjects with Advanced Solid Tumors” that characterizes the pharmacokinetic profile of Panitumumab in the Japanese population. The final study report should provide summary analyses and primary data, including pharmacokinetic data, in both the Japanese and non-Asian population that will permit an assessment of differences in pharmacokinetics, if any, based on race/ethnicity. The study will be completed (database lock) by June 30, 2006, and the final study report will be submitted by April 1, 2007.
Find even more information with a simultaneous search of Embase
Search extracted data in Safety, PK, Efficacy and ME&T modules. Or perform dedicated FAERS searches.
MET module content sources in detail...

- Unprecedented access to more than 300,000 lines of MET data extracted from FDA and EMA approval documents, FDA advisory committee meetings and journals for 4,485 drugs

Extracted information lets you limit search to specific parameters including:

<table>
<thead>
<tr>
<th>Metabolites</th>
<th>CYPs</th>
<th>Phase 2 Enzymes</th>
</tr>
</thead>
</table>
| Created, when available | Either involved in the metabolism or up/down regulated by the drug, quantitative and qualitative data | Examples include:  
- UDP-Glucuronosyltransferase  
- Acetyltransferase  
- Sulfoconjugating enzyme  
- Etc |

<table>
<thead>
<tr>
<th>Transporters</th>
<th>In Vitro</th>
<th>DDI Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>And drug effects on transporters</td>
<td><strong>Dynamic parameters</strong> such as CLint (Intrinsic Clearance) and Km (Michaelis Constant), Vmax (Maximum rate of reaction)</td>
<td>Ratio of AUC, Clearance, etc. in presence of another drug.</td>
</tr>
</tbody>
</table>

All with drug as: Substrate, inducer or inhibitor
What types of questions can be answered by MET?

**Scientific:**
- Which CYP/transporter production is likely stimulated when my drug is administered – which could result in an increase in the activity of these enzymes/transporters on other drugs?
- Which CYP/transporter production is likely inhibited when my drug is administered – which could result in a decrease in the activity of these enzymes/transporters on other drugs?
- Which CYPs/transporters are likely to act on my drug and metabolize it? At what rate? What effect does this have on the bioavailability of my drug within the proposed therapeutic window?

**Regulatory:**
- What level of mechanistic understanding of metabolizing enzymes and supporting experimental data is needed historically within my drug class to be approved?
- What mistakes have been made in this area in the past? What data has been sent back for clarification or with the demand for supplementary studies (drastically increasing time to market on a patented product)?
Example

• My drug is a substrate of CYP3A4.
  • What drugs inhibit/induce CYP3A4 and may have a DDI with my drug?
My drug is a substrate of CYP3A4. What drugs inhibit/induce CYP3A4 and may have a DDI with my drug?
Quickly get a list of all drugs that induce or inhibit CYP3A4, along with information on test system, dose, etc.

<table>
<thead>
<tr>
<th>ID</th>
<th>Drug</th>
<th>Parent/Metabolite</th>
<th>Substance Studied</th>
<th>Data Type</th>
<th>Enzyme/Transporter</th>
<th>Test System</th>
<th>Species</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>S-Methoxypsoralen</td>
<td>Parent</td>
<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>Liver, microsomes</td>
<td>Human</td>
<td>0.5-100 uM</td>
</tr>
<tr>
<td>2</td>
<td>S-Methoxypsoralen</td>
<td>Parent</td>
<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>AHII-1 T847 - cells, microsomes, recombinant</td>
<td>Human</td>
<td>0.1-100 uM</td>
</tr>
<tr>
<td>3</td>
<td>S-Methoxypsoralen</td>
<td>Parent</td>
<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>AHII-1 T847 - cells, microsomes, recombinant</td>
<td>Human</td>
<td>0.1-100 uM</td>
</tr>
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<td>4</td>
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<td>Parent</td>
<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>Microsomes, recombinant</td>
<td>Human</td>
<td>0.1-100 uM</td>
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<tr>
<td>5</td>
<td>S-Methoxypsoralen</td>
<td>Parent</td>
<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>Liver, microsomes</td>
<td>Human</td>
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<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>Liver, microsomes</td>
<td>Human</td>
<td>100 uM</td>
</tr>
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<td>7</td>
<td>S-Methoxypsoralen</td>
<td>Parent</td>
<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>Microsomes, recombinant</td>
<td>Human</td>
<td>0.1-100 uM</td>
</tr>
<tr>
<td>8</td>
<td>S-Methoxypsoralen</td>
<td>Parent</td>
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<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>Liver, microsomes</td>
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<td>9</td>
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<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>Microsomes, recombinant</td>
<td>Human</td>
<td>10-20,000 nM</td>
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<tr>
<td>10</td>
<td>S-Methoxypsoralen</td>
<td>Parent</td>
<td>Bergapten</td>
<td>Enzyme inhibitor (in vitro)</td>
<td>CYP3A4</td>
<td>Liver, microsomes</td>
<td>Human</td>
<td>10 uM</td>
</tr>
</tbody>
</table>
Drug-Drug Interaction Risk Calculator
Available with PK/MET modules

- DDIRC predicts potential metabolic Drug-Drug Interactions (DDIs) **between proprietary drugs and a panel of marketed drugs** automatically selected from the DDIRC library.

- DDIRC applies to orally-administered drugs* undergoing linear “**first-pass hepatic metabolism**” according to the “well-stirred” model.

- It does so based on a general **in vitro in vivo extrapolation (IVIVE)** method, using a mechanistic static model (MSM).

* Also applies to IV administered victim drugs with low clearance (i.e., low hepatic extraction ratio EH<0.3)
Search extracted data in Safety, PK, Efficacy and ME&T modules. Or perform dedicated FAERS searches.
Search using a wide range of Efficacy parameters

- Unprecedented access to more than 2.7 million lines of efficacy data extracted from FDA packages (current & historic) and EMA documents for 4,485 drugs

**Extracted information lets you limit search to specific parameters including:**

### Indication
**Includes:**
- In-house taxonomy
- Search by indication
- Filter results by indication type

### Endpoints
**Includes:**
- In-house taxonomy
- Filter by primary, secondary or other

### Study design:
**Includes:**
- Sample size
- Phase
- Study design
- Baseline
- Study population
- Comparative group

### Treatment:
**Includes:**
- Dose
- Placebo
- Route of administration
- Dose frequency

### Demographics
**Includes:**
- Study population
- Gender
- Age

### Species
**Includes:**
- Human
- Vertebrates
  - Birds
  - Fish
  - Mammals
  - Etc.
Multiple reasons are cited for clinical failures

Amongst the reasons:
• “insufficient proof of concept data”
• “Trial designs that are inconsistent with clinical endpoints”

Amongst the reasons:
• “…sponsor have failed to include adequate clinical data”
• “…which was non-specificity of the optimal drug dose.”
Late-stage failures consume resources (time & money)

- Improper endpoint selection
- Suboptimal patient populations
- Suboptimal dose regimen
- Efficacy benchmark not met
- Unanticipated adverse events

Chart:>
- >3 fold increase
- 2000: 0.8
- 2015: 2.6

Dollars (B)
The Efficacy Module helps impact translational and clinical development decisions…

• **Fail early**
  - Find comparative efficacy weaknesses early

• **Improve success rates**
  - Help to improve Phase I and Phase II clinical trial designs by potentially reducing risk of choosing suboptimal sample size, primary/secondary endpoint, study design, and other parameters

• **Improve selection of translational models**
  - Help to identity most appropriate preclinical models by leveraging human correlate data

• **Reduce regulatory cycling**
  - Prepare for more effective regulatory reviews to reduce cycling
Example

• Identify clinical and preclinical data that measures a specific endpoint
Mitigating the risk of efficacy-related failure “Did not meet primary endpoint”

• Of the top 13 Phase III failures highlighted by Genetic Engineering and Biotechnology News (GEN), **9 failed because they didn’t meet the primary endpoint**, 6 failed due to safety issues

• Use PharmaPendium to improve success rates of Phase I and II clinical trial designs by optimising selection of sample size, primary/secondary endpoint and study design

  ▪ Identify clinical and preclinical data that measures a specific endpoint
    - Search across drugs, drug classes, indications
    - Retrieve preclinical and clinical data
    - See details on study designs (type of study, dose regimen, etc.)
    - Compare with placebo data

Search for a specific endpoint(s)
Search for a specific endpoint(s)

Add Endpoints

- Cardiovascular
  - Clinical chemistry
    - Glycated hemoglobin (HbA1c)
      - Mean HbA1c

- Diabetes
  - Clinical chemistry
    - Fasting plasma glucose (FPG) and Glycated hemoglobin (HbA1c)
      - % of patients achieved and maintained control of blood glucose and HbA1c
    - Glycated hemoglobin (HbA1c)
      - % of subjects achieving an HbA1c level < 7.0%

Search on:

Endpoints
- Cardiovascular, Clinical chemistry, Glycated hemoglobin (HbA1c)
- Diabetes, Clinical chemistry response ...
- Diabetes, Clinical chemistry, Fasting p ...
- Diabetes, Clinical chemistry, Glycated ...
- Diabetes, Discontinuation/Compliance ...
- Diabetes, Time to response/Duration ...
- Diabetes, Treatment need, Dose up ...
- Diabetes, Treatment need, Rescue m ...
- Diabetes, Treatment need, Rescue m ...

Done
Search for a specific endpoint(s)

Efficacy data search
Show me preclinical & clinical studies for these:

Search criteria

Drugs
- Add drugs by drug class or drug name
- Add drugs by primary target or primary target class

Endpoints
- Cardiovascular, Clinical chemistry, Gly...
- Diabetes, Clinical chemistry, Fasting p...
- Diabetes, Discontinuation/Compliance...
- Diabetes, Treatment need, Dose up-tl...
- Diabetes, Treatment need, Rescue m...
- Endocrinology except diabetes, Clinica...
- Lipid metabolism disorders, Clinical c...

Search
Clear search
Search *across* drug classes

### Efficacy data search results

**29,470 records from Efficacy data:** Cardiovascular, Clinical chemistry, Glycated hemoglobin (HbA1c), Mean HbA1c (1) OR Diabetes (79150) OR Endocrinology

#### Refine search results:
- **Drugs**
- Routes of Administration
- Mono/Combination
- Sample size (#N)
- Indication Type
- Endpoints
- Phase
- Data provider
- Sources
- Study design
- Primary/Secondary
- Pathogens
- Dose Frequency
- Baseline
- Placebo
- Comparative Group

#### Table: Preclinical Data vs Clinical Data

<table>
<thead>
<tr>
<th>ID</th>
<th>Drug</th>
<th>Study Number</th>
<th>Phase</th>
<th>Mono/Combination</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acarbose</td>
<td>D96-004</td>
<td>Not specified</td>
<td>Combination</td>
<td>26 week, multi-center, randomized, double-blind, placebo controlled, two arm, parallel group comparison study</td>
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<td>Acarbose</td>
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<td>24 week study</td>
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<td>Monotherapy</td>
<td>randomized, double-blind, multi-center Italian placebo-controlled study</td>
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<td>633.0</td>
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<td>Monotherapy</td>
<td>double blind dose-response study</td>
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</table>
Search *across* drug classes

<table>
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<tr>
<th>ID</th>
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<td>Combination</td>
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<td>Not specified</td>
<td>Monotherapy</td>
<td>randomized, double-blind, multi-center Italian placebo-controlled study</td>
</tr>
</tbody>
</table>
Search *across* indications
See the lists of drugs where HbA1c is measured to quickly find PK, MET or Safety data
Use comparative data to optimise selection of sample size, endpoint and study design

Retrieve preclinical and clinical data

Easily retrieve placebo data

Look up information on clinical trial designs
Where Can you Learn More?

• Start with PharmaPendium Help – for answers to Frequently Asked Questions, Guides and links to archived webinar recordings

• [www.Elsevier.com/PharmaPendium](http://www.Elsevier.com/PharmaPendium) - for an overview on PharmaPendium and links to PharmaPendium content (Fact Sheets, Customer stories)

• In-Product Messaging gives links to the latest resources, news and upcoming webinars
Thank You!

- The recording and a link to the slides will be sent to you by email.
- For more information and questions please contact your regional office.
- Our next PharmaPendium webinar is not until January - refresh your memory with the year’s recorded webinars and slides, found in the PharmaPendium help section.
- Please fill out the survey that appears on your screen after leaving the webinar.

Any questions?
Thank you!

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