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R&D SOLUTIONS FOR PHARMA & LIFE SCIENCES

PharmaPendium®

Fact Sheet

Introduction

PharmaPendium improves the speed, success and confidence of critical drug development decisions on safety and efficacy, risk mitigation and study design, thanks to its unique collection of FDA and EMA regulatory resources and advanced search capabilities. It quickly pinpoints relevant information about drug safety, pharmacokinetics, efficacy, drug–drug interactions and risks to help scientists successfully assess the potential of their drug candidate.

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Access to comprehensive drug safety information, drug metabolism, clinical efficacy data and drug approval documents helps researchers answer critical questions and increases confidence in drug development decisions. PharmaPendium provides comparative regulatory-based evidence in a single database, informing critical drug development activities. Users gain access to almost 2.5 million searchable FDA and EMA regulatory documents, including reports from the FDA Advisory Committee and FDA Adverse Event Reports, and to extracted pharmacokinetic, efficacy, safety and metabolizing enzyme and transporter data.

Superior search capabilities and a powerful drug–drug interaction risk calculator make it easy to compare information across drugs and drug classes, reveal drug–drug interactions, track and compare post-market adverse events, and delve into the background of a drug's approval and adverse event history.

PharmaPendium impacts critical decisions

Industry analysis of FDA new molecular entity (NME) submissions indicates that nearly 50% of drugs fail to gain approval in the first regulatory cycle and that the median delay to approval is 435 days (1). Failing at that stage means losing more than a year's revenue and missing an opportunity to be the first to market. Even a delay in launching can cost a company as much as $4 to 5 million per day. At the same time, the industry struggles to improve R&D productivity (2). PharmaPendium users report improved speed, success and confident decision-making with PharmaPendium — all essential elements to getting best-in-class drugs to market faster.

Users agree that PharmaPendium helps them to (3):

- Inform product positioning against unmet safety and/or efficacy needs
- Improve the speed and success of regulatory submissions
- Have more confidence in go/no-go drug development decisions
- Avoid late-stage failure by averting safety and efficacy risks in clinical studies
- Reduce the required pre-clinical study volume by citing other relevant studies
- Validate the best animal models and predict how results will translate clinically

In a recent survey of PharmaPendium users (3), **90% of respondents recommend that their company continue to subscribe to PharmaPendium**, and the majority indicated that PharmaPendium is critical to their work, stating:

> "PharmaPendium provides important **insights that impact the success of a project**."
>
> "I can **find actionable information much faster** with PharmaPendium than with other methods."
>
> "PharmaPendium **facilitates comparative analyses** across drugs, targets, adverse effects and indications."

How does PharmaPendium deliver value?

PharmaPendium helps researchers to answer a range of questions, including:

- What safety, efficacy and DMPK data supports my analysis of in vitro and in vivo test results?
- How can I optimize my safety analyses and trial design based on existing drug information?
- How can I assess the pharmacokinetic properties of my drug candidate?
- Does my drug candidate present drug–drug interaction risks?
- What support can I get for making my case to the regulatory authorities?
- What are the efficacy benchmarks that must be met to compete?
- Which primary endpoints were used during Phase III clinical trials for similar drugs?
- Can I cite a previously run experiment for a similar drug in my approval submission?
- What post-market safety concerns should I be aware of?

It does this by supplying comprehensive, comparative, regulatory-based evidence in a single, easily searchable database.

PharmaPendium content

Content as of December 2017 includes:

>2.38M pages of FDA approval documents

>219K pages of EMA approval documents

>10.4M FAERS reports

>697K pages from FDA Advisory Committee Meetings

4,495 fully indexed and searchable drugs

>1.73M safety data lines

>319K metabolizing enzyme & transporter data lines

>1.65M pharmacokinetics data lines

Searching with PharmaPendium

PharmaPendium allows text-based searching with Boolean and proximity operators and synonym recognition; structure searching with structure similarity and substructure options; and browsing by categories such as drug name, class or target, or adverse effect and toxicity. The user interface presents 8 dedicated query areas to search or use predictive tools, each designed to facilitate specific drug development and pharmacovigilance workflows with extracted data and text results that are always linked back to source documents in case further investigation is needed.

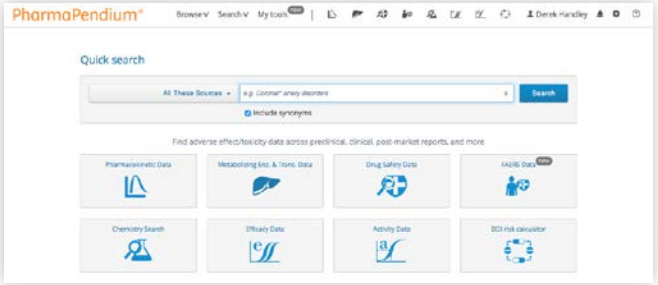


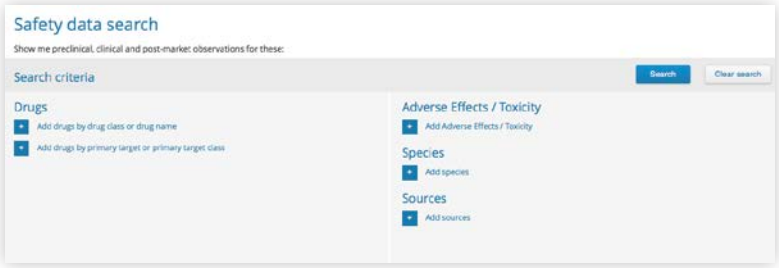
Figure 1. The PharmaPendium home screen

Assessment of drug safety

Fully text searchable FDA and EMA regulatory documents contain a wealth of comparative safety information on marketed drugs. For deeper, more precise searching across drugs, drug classes, adverse events and more, PharmaPendium includes detailed extracted safety information on parameters including adverse effect, toxicity, dose and species, with a link directly to the source data so users can understand the context of the extracted data.

The post-market safety data in PharmaPendium come from the FDA Adverse Event Reporting System (FAERS) and can be searched via the Drug Safety module (Figure 2) or through unique FAERS data searching functionalities (Figure 3A). All adverse effects in PharmaPendium are normalized by an expert content extraction team to MedDRA, enabling a unique translational view of data across the drug life cycle.

A



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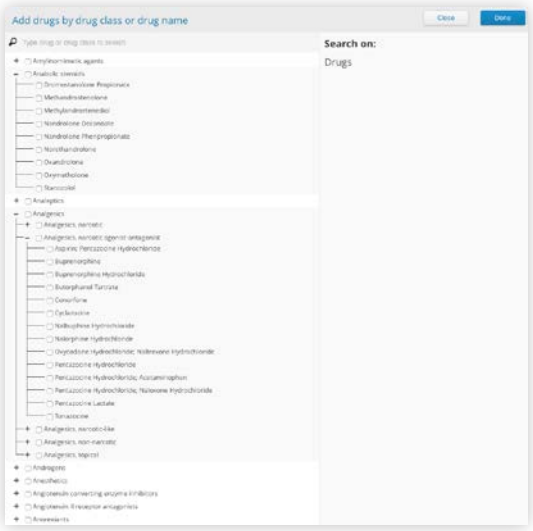


C

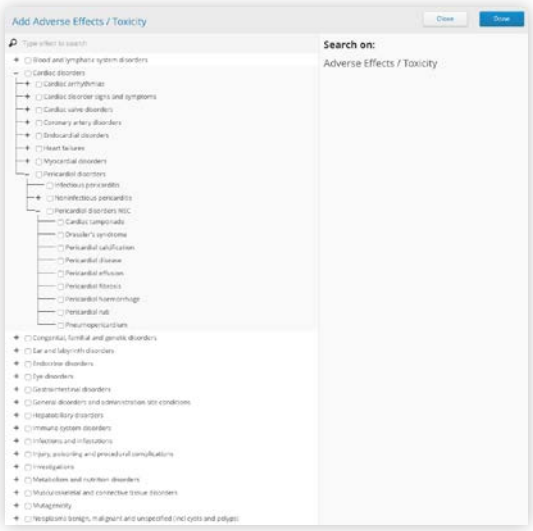


Figure 2. (A) PharmaPendium has a dedicated query form for safety data retrieval. Searchable menus enable quick selection of drugs (B) adverse effects (C), species and sources for the search, with drugs definable by class, name, primary target or primary target class.

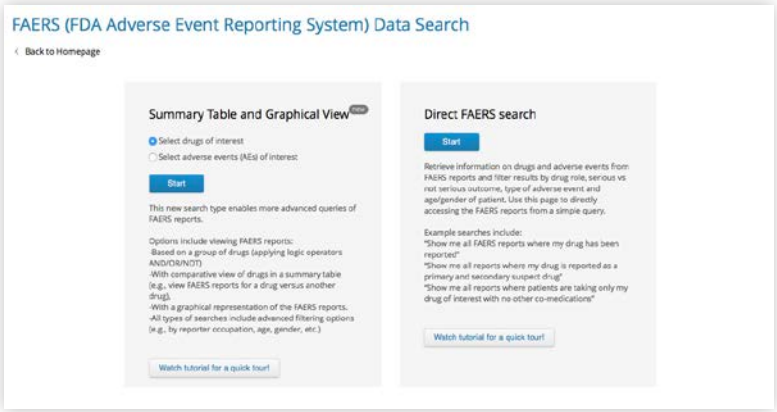
FAERS data searching

Spontaneous adverse event reporting systems, such as FAERS, represent a valuable source of real-world evidence about post-market drug safety. They allow rapid detection of signals and support an epidemiological approach to identifying adverse events that occur with low frequency, in populations not tested in clinical trials or over longer time periods. They also help to identify adverse events resulting from drug–drug or drug–food interactions.

With the PharmaPendium FAERS data searching functionality (Figure 3A), post-market reports can be specifically searched to compare and visualize adverse events reported for a drug or group of drugs and to find instances where a drug is reported as a primary suspect, secondary suspect, concomitant and/or interacting drug. Furthermore, results can be filtered using various parameters, including secondary suspect drug, type of adverse event, date range, age range, gender, seriousness of outcome, reporter occupation, and route of administration.

This type of detailed searching can provide additional insights into drugs suspected in adverse events and means users can more easily perform post-market signal detection and identify co-morbidities or potential DDIs not evident during clinical trials, helping to mitigate risk for new drugs in development and to make drugs safer post-market.

A



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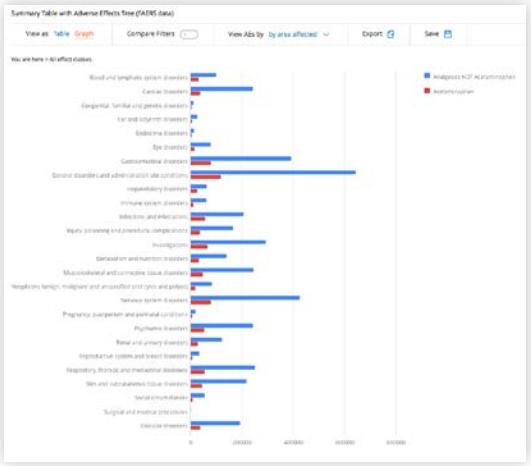

Figure 3. (A) The FAERS data search has two query types for investigating adverse events. Left panel: Users can build queries around self-defined drug groups (e.g., by role as primary or secondary suspect; with or without a co-medication) and apply filters, such as reporter occupation, seriousness of outcome, patient age, and date. Right panel: The direct FAERS search enables the identification of adverse events reported for a drug, drug class or indication and the retrieval of reports on drugs in any role. (B) Comparison of adverse events reported for a drug or drug group is also possible. Results of a comparative FAERS search are displayed in a convenient table or graphic format with links for drilling deeper and the possibility to apply filters.

Assessment of drug pharmacokinetics

Planning a successful regulatory approval strategy requires a deep understanding of the pharmacokinetic properties of a drug candidate within the context of the complete landscape of approved drugs. Essential data are contained in drug approval packages, but sifting through millions of lines of comparative data is resource intensive. Detailed, extracted pharmacokinetic information (Table 1) helps researchers find critical data from successful drug approvals in minutes.

Absorption	Binding	Biotransformation
• % absorbed	• Cell binding	• Enantiomeric ratio
• Bioavailability	• Protein binding	• Metabolic ratio
• Concentrations		• Metabolic stability
• Fraction absorbed		• Metabolic transformation
• Time values		

Distribution	Elimination	Species
• Accumulation	• Clearance	• Human
• Permeation	• Excretion values	• Birds
• Tissue distribution	• Half life	• Fish
• Volume of distribution	• Rate constants	• Mammals

Table 1. Extracted information enables limitation of the search to specific parameters. An overview of the types of parameter that can be selected for pharmacokinetics searches is shown.

Investigation of metabolizing enzymes and transporters

PharmaPendium's Metabolizing Enzymes and Transporters Module is a major resource for modeling drug–drug interactions. It provides a unique content source of unprecedented depth and curation for data on CYPs, Phase 2 Enzymes, Transporters and dynamic parameters, including CLint, Vmax and Km. Refine results by searching for a drug (or drug class) as an enzyme (or transporter) substrate, inhibitor or inducer and by searching for results on a specific enzyme or transporter.

Determination of drug efficacy

The PharmaPendium Efficacy Module (Figure 4) helps researchers rapidly find deeply enriched, comparative efficacy data extracted from FDA and EMA drug approval documents—data that is critical to successful early clinical programs and often extremely difficult to find. And with the integrated views of preclinical and clinical efficacy data, researchers can also answer questions that have a significant impact on Phase I/II study designs, saving valuable time and potentially getting to market faster.

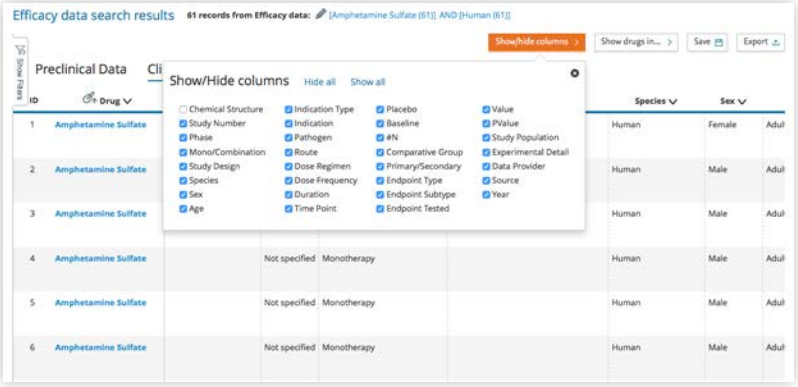

Figure 4. Results of an efficacy search. This search type can easily be refined using PharmaPendium's unique indication and endpoint taxonomies.

Prioritize drug candidates by predicting drug–drug interaction risk

PharmaPendium's DMPK Solution supports successful analysis and prioritization of drug candidates by helping to create a more detailed picture of potential drug–drug interactions (DDIs). Informed risk assessments are facilitated by comprehensive pharmacokinetic (PK) and metabolizing enzyme and transporter (MET) data from the respective PharmaPendium modules.

In addition, the solution provides a new DDI Risk Calculator, a mechanistic static model calculator that predicts drug–drug interaction risks in a manner compliant with the 2012 FDA draft Guidance for Industry Drug Interaction Studies. The DDI Risk Calculator allows rapid analysis of several drugs simultaneously, and provides a full risk profile of the potential for a drug candidate to interact with marketed drugs (Figures 5 and 6). Candidate drugs can be tested as victims or perpetrators with the possibility to enter a range of defining parameters. DDI prediction can be done very early in drug development, when only the metabolizing enzyme and % inhibition are known. As more data is gathered, additional values are used for the calculation that further refine predictions.

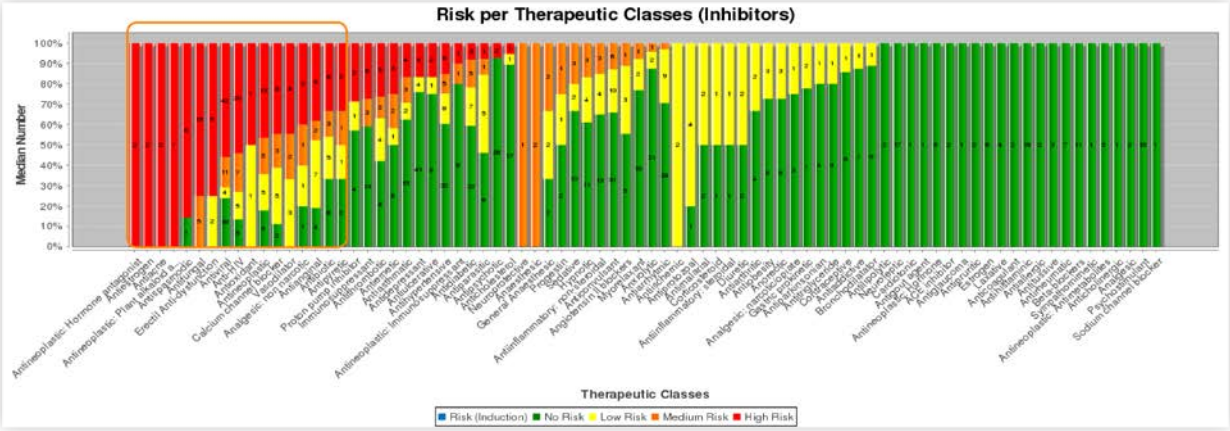

Figure 5. Simultaneous risk assessment of multiple drugs is possible. The orange box highlights the therapeutic drug classes with the highest risks.

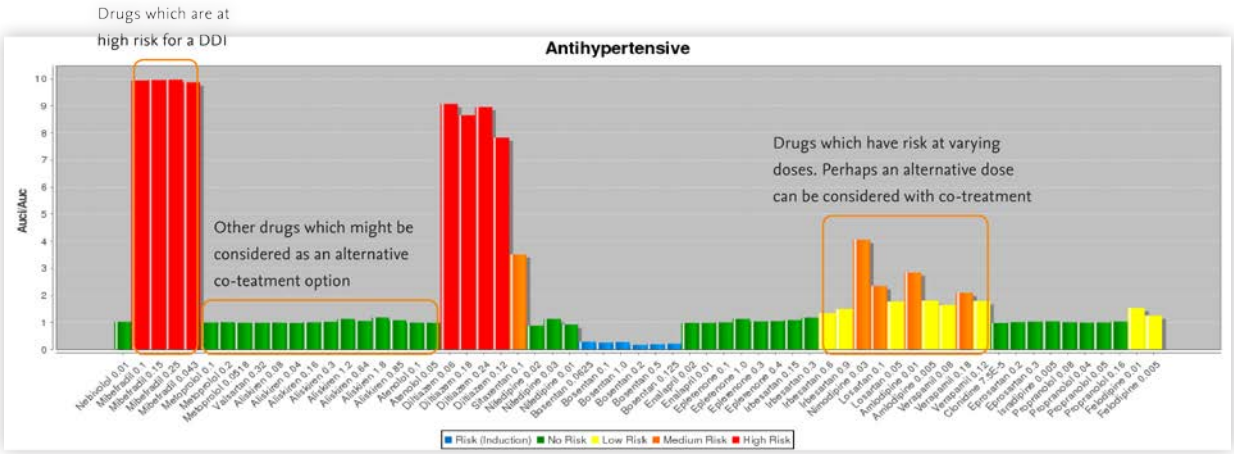

Figure 6. Visualization of DDI risk for drugs at varying doses quickly facilitates decision-making on co-treatment options.

References

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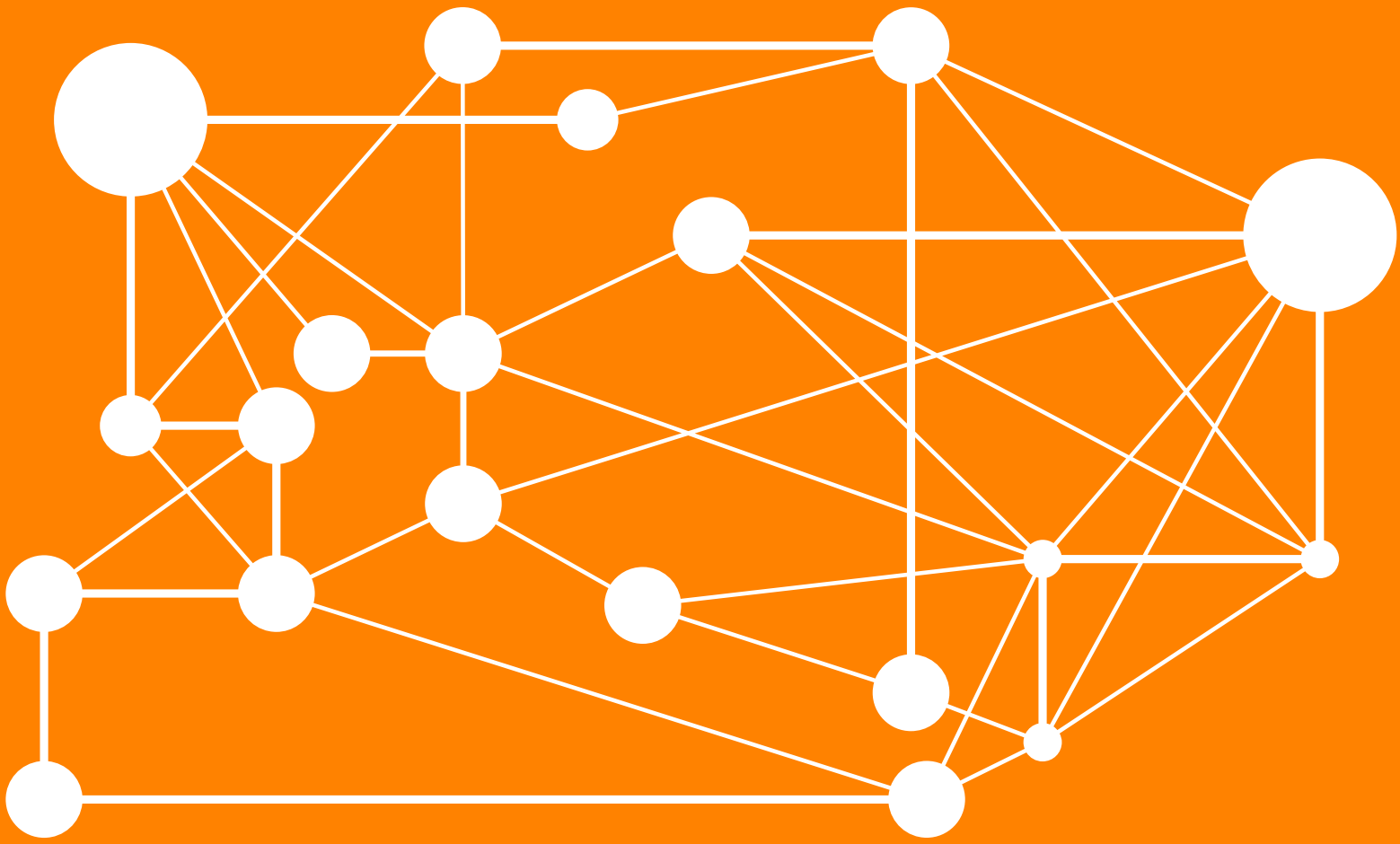
2. Paul, S.M., Mytelka, D.S., Dunwiddle, C.T., Persinger, C.C., Munos, B.H., Lindbord, S.R. and Schacht, A.L. 2010. How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nat. Rev. Drug Discov. 9(3), 203–214.
3. TechValidate Survey conducted on behalf of Elsevier, 2017. Details available on request.



PharmaPendium

PharmaPendium helps drug developers make more informed decisions about drug safety and efficacy, risk mitigation, and study design by providing searchable FDA and EMA drug approval documents and extracted data.

Learn More

To request information or a product demonstration, please contact us at elsevier.com/pharmapendium/contact-sales.

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