CERTARA

Drug Interaction Solutions

Transforming scientific data into clinical knowledge

Who we are

We are a team of pharmaceutical scientists, pharmacists, and clinicians who together bring over 180 years of cumulative expertise in drug metabolism, transport, pharmacokinetics (PK), drug interactions, and clinical pharmacology.

The Metabolism & Transport Drug Interaction Database program (now Drug Interaction Solutions) was founded at the University of Washington in the late 1990s, after recognizing the advances made in the field of *in vitro* to *in vivo* predictions and the need for more widespread knowledge about the risks of drug interactions. The program was acquired by Certara in June of 2023.

The database subscription program started in 2002. Over the years, the database content was expanded with the addition of pharmacogenetics, food-effect studies, organ impairment data, and additional mechanisms of PK-based drug interactions such as absorption-based interactions.

All curation activities and editorial tasks are performed in-house with a team that is dedicated to the overall platform, identified as the Drug Interaction Database (DIDB®), and user support.

MEET THE TEAM
DRUG INTERACTION SOLUTIONS

Isabelle Ragueneau-Majlessi, MD, MS, Co-Founder & Senior Director

Jingjing Yu, MD, PhD, Associate Director

Sophie Argon, PharmD, MS, Scientist

Katie Owens, BPharm, PhD, Scientist

Ichiko Petrie, PharmD, Scientist

Jessica Tay-Sontheimer, PhD, Scientist

Yan Wang, MS, Scientist

Christy Watson, MS, Associate Scientist

Cheryl Wu, PhD, Scientist

Marie C. Bodinier, MS, Marketing & Customer Experience

Chris Kinsella, Software Development

DRUG INTERACTION DATABASE LICENSING:
Contact: DIDBase@Certara.com

Our Recent Publications

SEEING WHAT IS BEHIND THE SMOKESCREEN: A SYSTEMATIC REVIEW OF METHODOLOGICAL ASPECTS OF SMOKING INTERACTION STUDIES OVER THE LAST THREE DECADES AND IMPLICATIONS FOR FUTURE CLINICAL TRIALS

Robert Hermann, Amin Rostami-Hodjegan, Ping Zhao, Isabelle Ragueneau-Majlessi
Clin Transl Sci. 2023 May;16(5):742-758

STRONG PHARMACOKINETIC DRUG-DRUG INTERACTIONS WITH DRUGS APPROVED BY THE US FOOD AND DRUG ADMINISTRATION IN 2021: MECHANISMS AND CLINICAL IMPLICATIONS

Jingjing Yu, Yan Wang, Isabelle Ragueneau-Majlessi
Clin Ther. 2022 Nov;44(11):1536-1544

EVALUATING THE FEASIBILITY OF PERFORMING PHARMACOGENETIC GUIDED-MEDICATION THERAPY MANAGEMENT IN A RETIREMENT COMMUNITY: A PROSPECTIVE, SINGLE ARM STUDY

Lena Chaitesipaseut, Jennifer Wilson Norton, Kristen Trivelli, Sophie M.A. Argon, Ichiko D. Petrie, Isabelle Ragueneau-Majlessi, Tamatha Mikes, Hao Nguyen, Beth Devine
J Am Coll Clin Pharm. 2022;5(3):291-301

PHARMACOKINETIC DRUG-DRUG INTERACTIONS WITH DRUGS APPROVED BY THE U.S. FOOD AND DRUG ADMINISTRATION IN 2020: MECHANISTIC UNDERSTANDING AND CLINICAL RECOMMENDATIONS

Jingjing Yu, Yan Wang, Isabelle Ragueneau-Majlessi
Drug Metab Dispos. 2022 Jan;50(1):1-7

EXPLORING THE RELATIONSHIP OF DRUG BCS CLASSIFICATION, FOOD EFFECT, AND GASTRIC PH-DEPENDENT DRUG INTERACTIONS

Katie H. Owens, Sophie M.A. Argon, Jingjing Yu, Xinning Yang, Fang Wu, Sue-Chih Lee, Wei-Jhe Sun, Anuradha Ramamoorthy,Lei Zhang, Isabelle Ragueneau-Majlessi
AAPS J. 2021 Dec 27;24(1):16

ANALYSIS OF DRUG-DRUG INTERACTION LABELING LANGUAGE AND CLINICAL RECOMMENDATIONS FOR NEWLY APPROVED DRUGS EVALUATED WITH DIGOXIN, MIDAZOLAM, AND S-WARFARIN

Lindsay M. Henderson, Claire E. Steinbronn, Jingjing Yu, Catherine K. Yeung, Isabelle Ragueneau-Majlessi
Clin Ther. 2021 Nov;43(11):2032-2039

What we offer

Drug Interaction Solutions (www.druginteractionsolutions.org) is designed to support research and regulatory scientists in their decision-making when evaluating PK-based drug-drug interactions (DDIs), gene-drug interactions, and drug safety.

→ Our main activity is the development of drug interaction content in DIDB®.

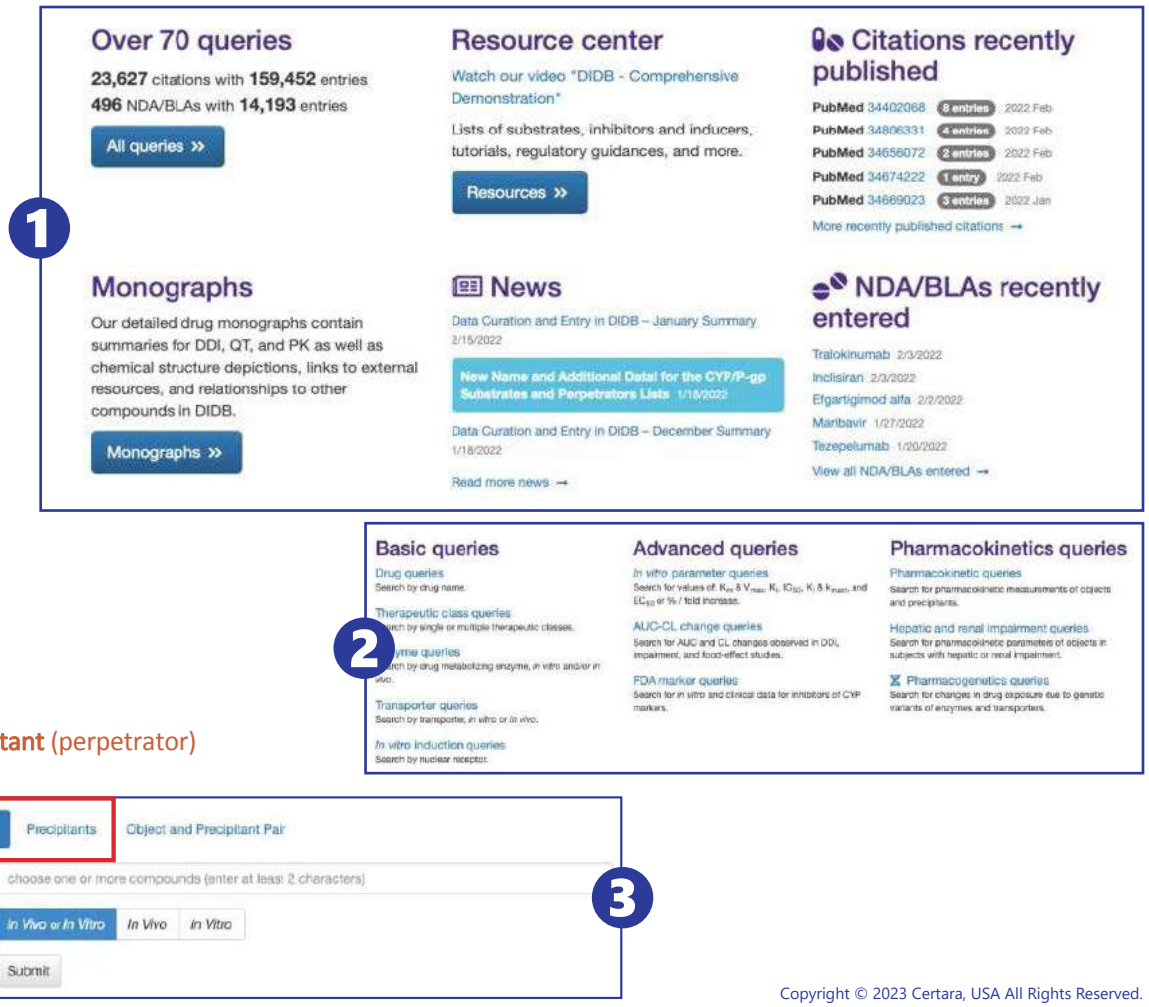
→ We also provide customized clinical PK datasets to fit specific solutions.

DIDB® has the largest manually curated collection of qualitative and quantitative human ***in vitro*** and clinical (***in vivo***) information related to various extrinsic and intrinsic factors. These include interacting co-medications, excipients, food products, herbals, tobacco, organ impairment, and genetics, that can affect drug exposure in humans. Its easy-to-use web portal allows users to efficiently retrieve the most relevant and up-to-date information from the large body of publications and regulatory documentation.

Information on drug disposition available in DIDB® encompasses:

- *In vitro* drug metabolism, transport, and DDIs (involving metabolizing enzymes, transporters, and their variants)
- Clinical DDIs and case reports
- Clinical pharmacogenetics
- Other DDI mechanisms including clinical absorption-based interactions (e.g., food-effect, pH-dependence, etc.)
- Clinical hepatic and renal impairment

EXAMPLE OF QUERY



CERTARA

Our expertise

In practice, we review the latest peer-reviewed publications as well as recent NDA/BLA reviews and drug labels from the FDA and select the content that is most relevant to support drug interaction evaluations at various stages of the drug development process.

We create detailed drug monographs that summarize the main mechanistic and quantitative findings including the drug characteristics, PK profile, DDI summary, QT summary, as well as information regarding the overall DDI risk level and label recommendations for clinical use.

We maintain an up-to-date Resource Center containing:

- A DDI Marker Studies Knowledgebase which includes known sensitive and moderate sensitive substrates,weak/ moderate/strong perpetrators, based on available clinical evaluations with marker compounds
- A series of tutorial videos and user guides which describe the content and the functionality of the database, and show how to best retrieve the information of interest
- Regulatory guidances from the FDA, EMA, PMDA, and Health Canada

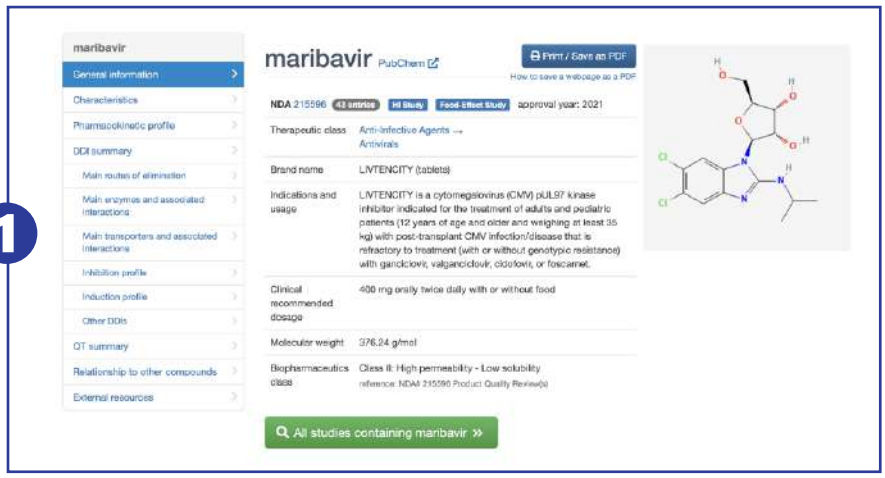
In addition to data curation, we share the results of our own research by contributing to workshops and conferences, and publishing articles and reviews on an ongoing basis.

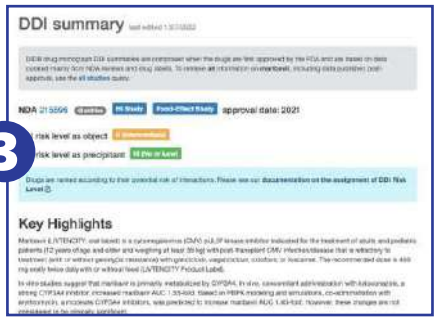
We work closely with colleagues from various universities, regulatory agencies, and pharmaceutical companies on the most pressing issues and challenges in the field.

We assist the end-users of DIDB® with highly specific and detailed database searches and outputs, breaking down often complex mechanisms of drug interactions to enable efficient problem solving.

We continuously expand the database content and improve its functionality based on user feedback.

DRUG MONOGRAPH





How we work

Selection of Citations

We identify the latest, most relevant publications and regulatory documents from NDA/BLA packages for manual curation.

Data Extraction

Prior to integration, the data is carefully and critically evaluated. When appropriate, and sometimes upon discussion with the study authors, comments are attached to the data. The richness of each citation is exploited, generating a highly detailed dataset. The data is formatted for immediate use and to allow meta-analysis of multiple sources.

Data Entry and validation

Once entered into the database, the data is validated by a second curator, who thoroughly reviews the studies and citations to make sure all the relevant information has been accurately extracted and represented. Only then, is the data released and accessible to end-users.

Data release

This process, built over more than 20 years, has been mastered by the team, and is highly-collaborative, allowing the database to be updated with new information daily, and the applications to be enriched with new scientific findings as soon as they become available.

Thorough standard operating procedures support the selection, distribution, data entry, and data validation of citations in DIDB®.

DIDB® BY THE NUMBERS

(as of August 2023)

PROGRAM ESTABLISHED

20
years ago

CITATION COVERAGE

1950
to present

OVER **70** queries INCLUDING
450 possible searches

20,000
total compounds

900
DDI summaries

DRUG-DRUG INTERACTIONS

PHARMACOKINETIC DATA FROM OVER

25,000
citations

INCLUDING

180,000
entries

550
NDAs/BLAs

INCLUDING

16,000
entries

Who are our users

PHARMACEUTICAL COMPANIES
Preclinical and clinical scientists working in drug development and regulatory groups

REGULATORY AGENCIES

ACADEMIC INSTITUTIONS

PUBLISHERS of DRUG INFORMATION

CONTRACT RESEARCH ORGANIZATIONS

NON-PROFIT ORGANIZATIONS

PROVIDERS of CLINICAL DECISION SUPPORT SYSTEMS

The worldwide userbase includes organizations of **all sizes**

Benefits

of using DIDB®

PROVIDE CONTEXT for the INTERPRETATION
of results obtained for candidate compounds

OPTIMIZE and VALIDATE PBPK MODELS
and static predictions

ASSIST with PRIORITIZATION and DESIGN
of clinical trials

GAIN INSIGHT on DDI RISK
and possible clinical outcomes

SUPPORT DRUG LABELING RECOMMENDATIONS
and the safe use of medications in various patient populations

PROVIDE CUSTOMIZED CLINICAL DATASETS AND EXPERTISE
to support personalized prescription applications

WHY SUBSCRIBE

The data we select and its presentation are unique reflections of our expertise in drug interactions. As a small and fully independent operation, we are flexible and react rapidly. We are able to continuously incorporate new scientific findings and improve the content and functionality of the database.

DIDB® is internationally recognized as an authoritative, unbiased, and transparent research tool. Our users have trusted our database for over 20 years.

FUTURE DIRECTIONS

With its mechanistic and quantitative features, and the breadth of its content, DIDB® has the potential to become a standard in supporting various healthcare applications and complex clinical decision algorithms. We believe that its integration into clinical tools for healthcare providers and patients is a next step in the development of Drug Interaction Solutions and will constitute a pivotal milestone in the management of adverse drug interactions in the clinic. We foresee that DIDB® content will help the emergence of new approaches in personalized medicine that aims at selecting the most appropriate drug and dose for each unique patient.

HONORS and AWARDS

DIDB® and its co-founders: Dr. René Levy and Dr. Isabelle Ragueneau-Majlessi have been selected to receive the 2022 Gary Neil Prize for Innovation in Drug Development.

> *"Your exemplary accomplishments and the superb drug interaction resource that you created" were noted by the ASCPT Awards Committee "as an exceptional achievement to facilitate drug development."*

Isabelle Ragueneau-Majlessi was also named a University of Washington CoMotion Presidential Innovation Fellow in 2015 for her work on the DIDB®. The prestigious fellowship program debuted in 2011 to foster entrepreneurial thinking across the University of Washington.

About Certara

At Certara, we accelerate medicines to patients, partnering with life science innovators. Together we advance modern drug development with biosimulation, regulatory science, and market access solutions.

For more information visit www.certara.com or email DIDBase@Certara.com