Clinical Organ Impairment Dataset
Transforming scientific data into clinical knowledge

The Clinical Organ Impairment Dataset contains study results from renal and hepatic impairment studies.

- **Detailed study information** regarding design, population, degree of organ impairment, drug dosing, PK, PD, and safety results are extracted from published articles (citations) and NDA reviews. Common metrics (percent changes in AUC, plasma concentrations, oral and renal clearance values) are used across all studies to allow metadata analysis of quantitative results.

- **Study results** are organized according to the overall effect and the severity of the disease:
  - Users can focus on a specific object drug or disease severity (mild, moderate, or severe)
  - Explicit changes in exposure can be searched
    (Example: “Find all drugs with at least 2-fold change in AUC in patients with a specific degree of impairment”)

- **Comprehensive PK parameters** for the object drug and its metabolites are available for each population studied and are compared to a healthy control population.

- **Several pre-formulated queries** allow users to retrieve the organ impairment dataset by drug name, changes in exposure, or disease severity, allowing users to compile and organize the large body of information available.

- **Results** can be viewed, customized, and downloaded in multiple formats, allowing users to compile and organize the large body of information available.
FROM A CITATION OR NDA/BLA REVIEW

The latest, most relevant, peer-reviewed publications and regulatory documents are identified and fully analyzed. Study protocol and results are manually curated to update the knowledgebase on a daily basis.
TO A FULLY CURATED DATASET

Prior to integration, all data are carefully and critically evaluated. The richness of each citation, including relevant insights, is exploited, generating a highly detailed dataset.

Tree View of Citation Data

Bazedoxifene shows an AUC increase of 327.3% in patients with severe hepatic impairment. What other drugs have an AUC change of at least 2-fold in these patients?
POWERFUL TOOL FOR DATA INTEGRATION: FROM ONE CITATION TO METADATA ANALYSIS

The data are formatted for immediate use and can be filtered and re-arranged to allow meta-analysis of multiple results.

Query all drugs exhibiting exposure increases of at least 2-fold in patients with severe hepatic impairment

<table>
<thead>
<tr>
<th>Object</th>
<th>Object Characteristics</th>
<th>Object Therapeutic Class</th>
<th>Object Administration</th>
<th>Object Dose</th>
<th>Object Internal</th>
<th>Population</th>
<th>AUC</th>
<th>Percent Change AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>atorvastatin</td>
<td>OPRSA unknown substance</td>
<td>Cancer Treatments — Kinase Inhibitors</td>
<td>Oral</td>
<td>200 mg</td>
<td>single dose</td>
<td>patients (N = 6 subjects with severe H [Child-Pugh class C])</td>
<td>98.10 (49.9) ngmL⁻¹h⁻¹</td>
<td>106.7</td>
</tr>
<tr>
<td>amlodipine</td>
<td>OPRSA unknown substance</td>
<td>Cancer Treatments — Kinase Inhibitors</td>
<td>Oral</td>
<td>10 mg (unknown)</td>
<td>once daily</td>
<td>patients (N = 6 subjects with severe hepatic impairment [number of subjects/doses not provided])</td>
<td>451.86 (5.04) h</td>
<td>442.3</td>
</tr>
<tr>
<td>amlodipine</td>
<td>OPRSA unknown substance</td>
<td>Cancer Treatments — Kinase Inhibitors</td>
<td>Oral</td>
<td>50 mg</td>
<td>single dose</td>
<td>patients (N = 8 subjects with severe hepatic impairment [Child-Pugh class C])</td>
<td>1169.0 (53.8) ngmL⁻¹h⁻¹</td>
<td>987.3</td>
</tr>
<tr>
<td>amlodipine</td>
<td>OPRSA unknown substance</td>
<td>Cancer Treatments — Kinase Inhibitors</td>
<td>Oral</td>
<td>50 mg</td>
<td>single dose (capsule)</td>
<td>patients (N = 8 subjects with severe hepatic impairment [Child-Pugh C; score 10-13])</td>
<td>1169.0 (53.8) ngmL⁻¹h⁻¹</td>
<td>416.1</td>
</tr>
</tbody>
</table>

Obtain a complete list of drugs that may need dosing adjustment in patients with severe hepatic impairment

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APPLICATIONS OF CLINICAL ORGAN IMPAIRMENT DATASET

PROVIDES CONTEXT for RESULTS OBTAINED with candidate compounds

HELPS DEVELOP OVERALL REGULATORY STRATEGY and optimize renal and hepatic impairment trials:
- Guides choice of appropriate study design
- Refines inclusion/exclusion criteria for control population and patients with organ impairment
- Helps select dose regimen of object drug
- Provides PK variability data for power calculations

SUPPORTS PBPK MODELING and SIMULATIONS with drug and disease parameters, changes in exposure validation set

ACCESS REGULATORY ORGAN IMPAIRMENT STUDIES for recently marketed drugs

PROVIDES REFERENCE RESOURCE for ASSESSMENT of DRUG SAFETY in patients with different severity of renal or hepatic function deficiency

CLINICAL ORGAN IMPAIRMENT DATASET IN NUMBERS

(as of October 16, 2023)

RENAL IMPAIRMENT
- 1,169 citations
- 3,688 entries
- 302 NDAs/BLAs
- 849 entries

HEPATIC IMPAIRMENT
- 688 citations
- 1,715 entries
- 290 NDAs/BLAs
- 715 entries

Dedicated organ impairment queries with 123 possible searches

1,090 possible searches drugs evaluated in organ impairment studies
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