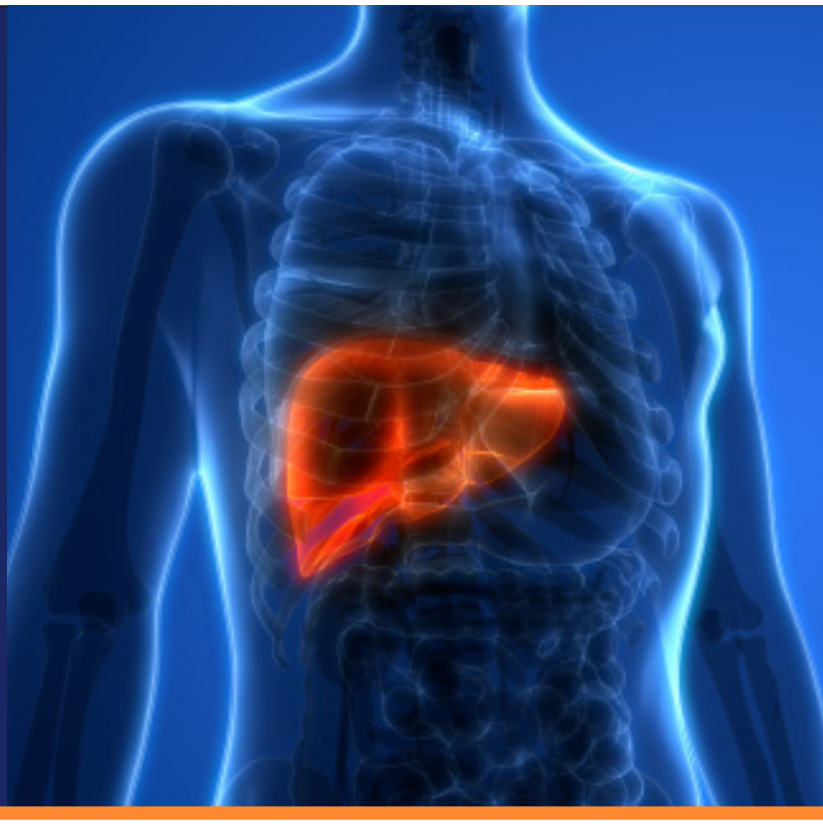
# IQ DRUG-INDUCED LIVER INJURY (DILI) INITIATIVE

An Affiliate of the International Consortium for Innovation and Quality in Drug Development

## Background

Monitoring and diagnosing drug-induced liver injury (DILI) in clinical trials and new drugs presents a critical challenge to the pharmaceutical industry and patient care. Hepatotoxicity has been the most frequent single cause of drug marketing safety withdrawals for the past 50 years, and is the most common cause of aborted drug development.

Until the establishment of IQ-DILI in June 2016, there had been no industry-led effort focusing on clinical aspects of DILI, which are not sufficiently covered by existing guidance.



## Member Benefits

A collaborative initiative was launched in the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ) to tackle the challenges of DILI.

Participation in IQ-DILI enables member companies to:

- **Define and share** best practices for the detection, monitoring, management and prevention of DILI in clinical trials and post-marketing pharmacovigilance programs.
- **Engage** in cross-company clinical data-sharing to substantiate and advance best practices.
- **Create** a capability to allow evaluation, prioritization, and execution of research concepts of interest to IQ-DILI.
- **Address** gaps in best practices and current guidelines related to DILI.
- **Collaborate** with key stakeholders and experts in the field, including regulators, academics, and other industry DILI collaborators. Representatives from over 20 different organizations and academic institutions have participated in IQ-DILI meetings.

## Members

AbbVie
AstraZeneca
Bayer
Bristol Myers Squibb
Eli Lilly
EMD Merck Serono
Gilead
Genentech
GlaxoSmithKline
Janssen
Novartis
Otsuka
Pfizer
Sanofi
Takeda
Theravance

# IQ-DILI Impact

Activities of the IQ-DILI working groups include conducting industry benchmarking, developing data sharing research questions, and authoring best practice papers. The Working Groups are focused on best practices for:

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| Abnormal Baselines | Monitoring and assessment of potential DILI in patients with abnormal hepatic biochemical tests at baseline |
| Immunotherapy | Assessing immune-related liver injury due to immunotherapy, including checkpoint inhibitors or other biologics |
| Nonclinical Translation | Adjustments in monitoring and assessment of DILI during clinical trials based on nonclinical toxicology findings |
| Pediatrics | Addressing DILI in clinical trials and in post-marketing pharmacovigilance activities in the pediatric (including neonatal) population |
| Causality Assessment | Causality assessment in all patterns of DILI (hepatocellular, cholestatic, hepatic steatosis, vascular) and best practices for drug re-challenge |
| Biomarkers | Investigating emerging, potentially translational biomarkers for the assessment of DILI |
| Risk Mitigation & Pharmacovigilance | Post-marketing pharmacovigilance programs and Risk Evaluation and Mitigation Strategies (REMS) for DILI |
| Immunosuppression | Monitoring, prevention, and management of Hepatitis B virus reactivation during the development of immunosuppressing drugs |
| DILI in Elderly | Addressing knowledge gaps and proposing recommendations for future research on DILI in the geriatric population |

# Recent Publications


Regev, A., Palmer, M., Avigan, M. I., Dimick-Santos, L., Treem, W. R., Marcinak, J. F., Seekins, D., Krishna, G., Anania, F. A., Freston, J. W., Lewis, J. H., Sanyal, A. J., & Chalasani, N. (2019). "Consensus: guidelines: best practices for detection, assessment and management of suspected acute drug-induced liver injury during clinical trials in patients with nonalcoholic steatohepatitis." Aliment Pharmacol Ther, 49(6), 702-713. doi:10.1111/apt.15153

Roth, S. E., Avigan, M. I., Bourdet, D. , Brott, D. , Church, R. , Dash, A. , Keller, D. , Sherratt, P. , Watkins, P. B., Westcott-Baker, L. , Lentini, S. , Merz, M. , Ramaiah, L. , Ramaiah, S. K., Stanley, A. M. and Marcinak, J. (2019), "Next-Generation DILI Biomarkers: Prioritization of Biomarkers for Qualification and Best Practices for Biospecimen Collection in Drug Development." Clin Pharmacol Ther, 107(2), 333-346. doi:10.1002/cpt.1571

Palmer, M., Regev, A., Lindor, K., Avigan, M. I., Dimick-Santos, L., Treem, W., Marcinak, J., Lewis, J.H., Anania, F.A., Seekins, D., Shneider, B. L., and Chalasani, N. (2020). "Consensus guidelines: best practices for detection, assessment, and management of suspected acute drug induced liver injury occurring during clinical trials in adults with chronic cholestatic liver disease." Aliment Pharmacol Ther, 51(1), 90-109. doi:10.1111/apt.15579


## Contact Us

If you are interested in learning more about IQ-DILI, its impactful work, and how to get involved, please contact the IQ-DILI Secretariat.


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Learn more about IQ-DILI at www.iqdili.org