

# Hepatocyte-based in vitro model for drug-induced cholestasis

*Commonly used acronym: DICI-MODEL*

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## SCOPE OF THE METHOD

<b>Alternative method relates to</b>	Human health
<b>Alternative method is situated in</b>	Translational - Applied Research
<b>Type of alternative method</b>	In vitro - Ex vivo
<b>This method makes use of</b>	Human derived cells / tissues / organs
<b>Specify the type of cells/tissues/organs</b>	Human liver tissue (from resections during surgery)

## DESCRIPTION

### Method keywords

bile acids

sandwich-cultured human hepatocytes

in vitro model

### Scientific area keywords

Hepatotoxicity

Drug-induced liver injury (DILI)

Drug-induced cholestasis

### Method description

Sandwich-cultured hepatocytes are exposed to test compounds (e.g. drug candidates) or known hepatotoxicants (as controls) both in the absence and in the presence of a mixture of physiologically relevant bile acids. After 24h, decreased hepatocyte viability and functionality in the presence of bile acids is expressed as a drug-induced cholestasis index (DICI) value. DICI values < 0.8 are indicative of possible cholestatic liabilities and a safety margin can be calculated provided *in vivo* therapeutic exposure data (or estimates) are available.

### **Lab equipment**

Biosafety cabinet,  
Plate reader (absorbance),  
Incubator.

### **Method status**

Internally validated  
Published in peer reviewed journal

### **PROS, CONS & FUTURE POTENTIAL**

#### **Advantages**

Early detection of cholestasis potential of medicines and environmental toxicants.

#### **Challenges**

Availability and characterisation of plateable human hepatocytes.

#### **Modifications**

Additional endpoints (ATP instead or urea, bile acid profiles) are under development.

#### **Future & Other applications**

Could extrapolate concept of co-incubation with endogenous compounds to other organs / tissues.

### **REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION**

#### **References**

Chatterjee S, Richert L, Augustijns P, Annaert P. Hepatocyte-based in vitro model for assessment of drug-induced cholestasis. *Toxicol Appl Pharmacol*. 2014 Jan 1;274(1):124-36. doi: 10.1016/j.taap.2013.10.032. Epub 2013 Nov 7. PubMed PMID: 24211272.

Chatterjee S, Richert L, Augustijns P, Annaert P. Hepatocyte-based in vitro model for assessment of drug-induced cholestasis. *Toxicol Appl Pharmacol*. 2014 Jan 1;274(1):124-36. doi: 10.1016/j.taap.2013.10.032. Epub 2013 Nov 7. PubMed PMID: 24211272.

Oorts M, Baze A, Bachellier P, Heyd B, Zacharias T, Annaert P, Richert L. Drug-induced cholestasis risk assessment in sandwich-cultured human hepatocytes. *Toxicol In Vitro*. 2016 Aug;34:179-186. doi: 10.1016/j.tiv.2016.03.008. Epub 2016 Apr 2. PubMed PMID: 27046439.

## Associated documents

### Links

[Link to initial publication on this topic](#)

## PARTNERS AND COLLABORATIONS

### Organisation

**Name of the organisation** KU Leuven

**Department** Pharmaceutical and Pharmacological Sciences

**Country** Belgium

**Geographical Area** Flemish Region

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