

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

**Commonly used acronym:** DICI-MODEL

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### Organisation

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**Country** Belgium

**Geographical Area** Flemish Region

## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Translational - Applied Research
<b>Type of method</b>	In vitro - Ex vivo
<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 of 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.

### Links

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

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