

# The detection of cholestasis-inducing agents in cultured primary rat hepatocytes

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## Organisation

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**Department** Pharmaceutical and Pharmacological Sciences

**Specific Research Group or Service** In Vitro Toxicology and Dermato-Cosmetology

**Country** Belgium

**Geographical Area** Brussels Region

## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Basic Research, Translational - Applied Research
<b>Type of method</b>	In vitro - Ex vivo
<b>Species from which cells/tissues/organs are derived</b>	Rat
<b>Type of cells/tissues/organs</b>	Primary rat hepatocytes

## DESCRIPTION

### Method keywords

Sandwich cultures

Hepatocytes

Bile salt export pump (Bsep) inhibition

Cholyl-lysyl-fluorescein (CLF)

Cholestasis-inducing potential

### **Scientific area keywords**

Toxicology

in vitro

Drug-induced liver injury (DILI)

cholestasis

### **Method description**

The standard operating procedure describes a method to assess the cholestasis-inducing potential of chemicals, in casu in cultures of primary rat hepatocytes. The procedure relies on the accumulation of the fluorescent bile salt export pump (Bsep) substrate cholyl-lysyl-fluorescein (CLF) in the canalicular network of sandwich-cultured rat hepatocytes either in presence or the absence of Bsep inhibitors.

### **Lab equipment**

Fluorescent microscope (Nikon Eclipse Ti-S, Belgium)

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

### **Advantages**

The standard operating procedure comprises an easy-to-apply method to detect cholestasis-inducing agents based on Bsep inhibition. Since sandwich cultures of hepatocytes, in contrast to conventional monolayer cultures, exhibit reformation of the canalicular network and polarized excretory functions, this culture systems forms an appropriate experimental setting for studying biliary excretion.

### **Challenges**

Most Bsep substrates, including CLF, cannot undergo efficient cellular translocation without the support of an uptake transporter, such as sodium-dependent taurocholate cotransporting polypeptide (Ntcp). A number of drugs, known to inhibit Bsep activity, also possess the ability to interfere with the Ntcp-mediated uptake of

bile salts. This phenomenon should always be taken into account as it may complicate the interpretation of the experimental results.

## REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

### References

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### Associated documents

[BSEP inhibition.docx](#)

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