

## PRODUCT SPECIFICATIONS

# UNDIFFERENTIATED HEPARG<sup>®</sup> CELLS CRYOPRESERVED

CATALOG NUMBER: HPR101

*For in vitro and research use only*

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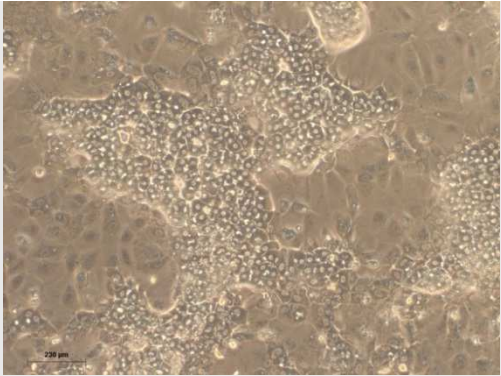
For more information, visit  
[www.HepaRG.com](http://www.HepaRG.com)

## 1. PRODUCT DESCRIPTION

<b>Species</b>	Human	
<b>Origin</b>	Liver tumor of a patient suffering from hepatocarcinoma and hepatitis C infection	
<b>Safety data</b>	Absence of hepatitis B, hepatitis C and HIV1 viruses checked by PCR on the cell suspension. <i>Caution: although controls are performed, human material has to be considered as potentially dangerous. Take maximum care in order to protect yourself and your colleagues.</i>	
<b>Biosafety level</b>	2	
<b>Description</b>	HepaRG <sup>®</sup> cells are human hepatic progenitor cells able to give rise to adult fully differentiated hepatocytes in appropriate culture conditions. HepaRG <sup>®</sup> cells have the unique properties of maintaining significant levels of hepatocyte functions, of being CYP450 inducible and supporting the complete replicative cycle of HBV. Catalog number HPR101 corresponds to a frozen vial of undifferentiated HepaRG <sup>®</sup> cells at passage P12. <b>Available only after a license agreement made with Biopredic International (for commercial companies) or under a MTA made with Inserm (for non-profit organisations).</b> Gripon P. <i>et al. Proc. Natl. Acad. Sci. 99, 15655-15660, 2002.</i>	
<b>Packaging</b>	0.5 mL vial with at least 1 x 10 <sup>6</sup> viable cells	
<b>CYP genotyping data</b>	Obtained in collaboration with N. Picard at Limoges hospital (France) using a validated TaqMan allelic discrimination assay (ABI PRISM 7000 Sequence Detection System, Applied-Biosystems).	
<b>SNPs description</b>	<b>CYP2D6</b>	
SNPs: Single Nucleotide Polymorphisms wt: wild- type mut: mutation **: wt=G T=minor allele in Caucasians	*2 (2850C>T)	*2/wt
	*3 (2549delA)	wt/wt
	*4 (1846G>A)	wt/wt
	*7 (2935A>C)	wt/wt
	*10 (100C>T)	wt/wt
	<b>CYP3A4</b>	
	*1B (392G>A)	wt/wt
	<b>OATP1B1 (=OATP2)</b>	
	*5 (521T>C)	wt/*5
	<b>OATP1B3 (=OATP8)</b>	
334T>G	wt/wt**	
<b>MRP2</b>		
-24C>T	wt/wt	
1249G>A	wt/mut	
3972C>T	wt/mut	

## 2. CHARACTERIZATION OF PRODUCT

### Cell controls

Criteria	Method	Specification
<b>Number of viable cells per vial</b>	Microscopic observation	$\geq 1 \times 10^6$
<b>Post-thaw viability *</b>	Trypan blue exclusion test	$\geq 80 \%$
<b>Cell morphology</b>	Microscopic observation at passage n°14 after 2 weeks in the HepaRG® Growth Medium using ADD710, and 2 weeks in the HepaRG® Differentiation Medium using ADD720. 50 % of typical hepatocyte-like cells are organized in well-delineated clusters with bright canaliculi-like structures.	 <b>X 100- August 07, 2014</b>
<b>Mycoplasma detection</b>	Biochemical test	Negative
<b>Microbial sterility</b>	Under standard use conditions	No microbial growth detectable

\*: After thawing, undifferentiated HepaRG® viability is determined by Trypan blue (0.05% in PBS) exclusion test at 10 min post-thaw.

### **Vmax value of Phase I dependent activities (nmole/h/mg proteins)**

Activity	Enzyme	Method
Phenacetin O-deethylase activity	CYP1A2	After 2 weeks in the HepaRG® Growth Medium using ADD710, and 2 weeks in the HepaRG® Differentiation Medium using ADD720, cells were incubated for 1 hour at 37°C in MEM medium with the following test substrates: <ul style="list-style-type: none"> <li>- phenacetin (200µM),</li> <li>- midazolam (50µM),</li> <li>- bupropion (100µM),</li> <li>- dextrometorphan (100µM).</li> </ul> Metabolites formed were measured by LC-MS/MS.
Midazolam 1' hydroxylase activity	CYP3A4/5	
Bupropion hydroxylase activity	CYP2B6	
Dextrometorphan O-demethylase activity	CYP2D6	

### **Characterization of phase II enzymes (nmole/h/mg proteins)**

Activity	Enzyme	Method
Paracetamol glucuronidation	UGT1A1 UGT1A4 UGT1A6	After 2 weeks in the HepaRG® Growth Medium using ADD710, and 2 weeks in the HepaRG® Differentiation Medium using ADD720, cells were incubated for 5 hours at +37°C in MEM medium with 1mM paracetamol. Metabolites formed were measured by LC-MS/MS.
Paracetamol sulfation	SULT1A1 SULT1A3/4 SULT2A1	

### 3. CONDITIONS OF STORAGE AND DELIVERY

STABILITY, STORAGE, DELIVERY	
<b>Stability and Storage</b>	5 years in liquid nitrogen
<b>Delivery</b>	In dry ice
<b>Use</b>	Follow instruction manual for HepaRG® cell line culture.

### 4. COMPANION PRODUCTS

CULTURE MEDIA*	
Denomination	Catalog number
HepaRG® Growth Medium supplement with antibiotics, to be combined with 500 mL of Basal medium	ADD710
HepaRG® Differentiation Medium supplement with antibiotics, to be combined with 500 mL of Basal medium	ADD720

*For details on preparation of culture media, follow instruction manual for HepaRG® cell line culture*

### 5. OTHER OFFERING OF THE HEPARG® CELLS

Denomination	Catalog number
HepaRG® differentiated cells, cryopreserved after differentiation using a proprietary process developed by Biopredic International.	HPR116
HepaRG® differentiated cells, cryopreserved, using a proprietary freezing process developed by Biopredic International that allows direct thawing and seeding of the differentiated cells without the need for post-thaw washing, centrifugation and counting steps.	HPR116NS
HepaRG® undifferentiated cells, cryopreserved with a sufficient quantity of culture medium for production of 50 plates within a 6 month period of time.	KIT901