**Volume-dependent HepaRG® Human Hepatic Cell**

**Propagation and Use Sublicense**

This Agreement is between**:**

**BIOPREDIC INTERNATIONAL,** a company registered in France (registered number B 391 701 232) whose registered office is situated at Parc d’Affaires La Bretèche, Bât A4, 35760 Saint Gregoire - France (“BI”); and

Organization (“ORG”)\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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Whose Principal Scientist (“PS”) is:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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Complete address of facility at which HepaRG cells will be used (“Site”) (if different from above):

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**WHEREAS:**

* 1. BI is granted with exclusive, unrestricted worldwide rights to HepaRG cells (HepaRG) under patent rights owned by the French National Institute for Health and Medical Research (as referred and more detailed herein as to “INSERM Patents”) claiming for “Novel human hepatoma lines, methods for obtaining same and uses thereof”;
  2. BI has developed media supplements for the production, culture, and use of the HepaRG Cells (“HepaRG Media”) for drug discovery, drug development, pharmacology and toxicology, production of biomarkers and drug metabolites, and related services;
  3. ORG desires to obtain a sublicense from BI in order to produce and use fresh plated HepaRG and to use HepaRG Media (collectively, “Products”) at the Site by its PS. BI desires to grant ORG a sublicense for that purpose (“Use”) under terms and conditions of this Agreement.

When interpreting this Agreement:

unless the context otherwise requires, all references to a particular Paragraph or Schedule shall be a reference to that Paragraph or Schedule in or to this Agreement as it may be amended from time to time;

the headings are inserted for convenience only and shall be ignored when construing this Agreement;

## unless the contrary intention appears, words importing the masculine gender shall include the feminine and *vice versa* and words in the singular include the plural and *vice versa*;

### the words “include”, “included”, and “including” are to be construed without limitation to the generality of the preceding words; and

### reference to any statute or regulation includes any modification or renewal of that statute or regulation.

### GRANT OF SUBLICENSE

BI hereby grants to ORG a sublicense for Use of Products at the Site and by the PS; ORG and PS will be entitled to produce and use fresh plated HepaRG, and use HepaRG Media (listed on Schedule 1), at the Site and by the PS solely as provided herein. This Agreement shall become effective as of the last date of its execution (Effective Date). The term of this Agreement is for one year, provided that the term will automatically be extended for subsequent one-year periods unless one Party notifies the other of its desire to cancel this Agreement, which notice must be delivered no later than ninety (90) days prior to the subsequent anniversary of the Effective Date.

## ORG shall have no right to sublicense any of the rights sublicensed under this Agreement and agrees that use of the Products will be limited to use only as a research reagent. ORG further agrees that Products will not :

#### be administered to animals nor humans;

#### be re-sold, transferred, shipped, or donated to anyone outside the Site ; or

#### be used as a direct means of production or manufacture of commercial products, cDNA libraries, or cell lines.

#### **ACCESS TO AND USE OF PRODUCTS**

Promptly after the Effective Date, ORG shall provide a purchase order or other authorization to BI for initial shipment of ADD71x Growth Medium Supplement ; and ADD72x, Differentiation Medium Supplement in volumes to be determined by ORG, but in no case shall the initial volume be less than three (3) bottles of each. BI will invoice ORG based on the number of bottles shipped using the prices listed on Schedule 1, plus shipping and handling. Upon receipt of full and accurate payment of such invoice, BI will ship one vial of undifferentiated HepaRG Cells to be used by ORG for its purposes in compliance with this Agreement. The delivery of the vial of HepaRG Cells and bottles of Media shall not release ORG from its obligations under this Agreement.

In addition to its initial shipment of Products to ORG in accordance with ORG’s order and this Agreement, BI shall also provide to PS BI’s then-current Standard Operating Procedures for HepaRG, and Use Recommendations.

ORG shall use only HepaRG Media with the HepaRg cells, to the exclusion of any other culture medium but with the sole exception of media used as a vehicle to carry or maintain test article introduced to the HepaRG cells. ORG acknowledges that BI is agreeing to exempt ORG from a sublicense fee in consideration of ORG’s full-faith commitment to utilize only HepaRG Media as provided herein. ORG further acknowledges that it is in its own interest to comply with this provision in order for BI to minimize its support and assistance expenses and hence ORG’s expenses, which expenses and demands BI reasonably expects would increase dramatically if non-HepaRG media is used (except as provided herein). Use of non-HepaRG media (except as provided herein) shall be considered as an immediate and *prima facie* authorization by ORG to pay a full license fee in the amount of 100,000euros/year. The license fee shall be calculated based on the number of years between the Effective date of this Agreement and the recognition of ORG’s violation of this provision, without proration for partial years.

#### During the term of this Agreement, ORG shall order a minimum of three additinal bottles of ADD71x and three additional bottles of ADD72x during every full, three-month period following receipt of the initial shipment (Minimum Quarterly Order). For avoidance of doubt, if the initial shipment of Media was received in mid-May, ORG is hereby obligated to order at least three bottles each of ADD71x and ADD72x during the period of June through August. In the event of a failure by ORG to place a Quarterly Order, ORG agrees that BI shall have the right to issue an invoice in an amount equal to the Minimum Quarterly Order, and that ORG shall pay such invoice in full according to the terms of this Agreement.

## During the term of this Agreement, BI shall have the right to increase prices for HepaRG Media; increases in an amount exceeding 4% shall be announced to ORG no later than 120 days preceding the subsequent anniversary of the Effective Date of this Agreement.

## GENERAL PROVISIONS

### ORG shall take all necessary steps to ensure the proper and safe handling, storage, and use of Products in accordance with all applicable laws, rules and regulations and expressly acknowledges that, as biologic materials, it will ensure Products are handled using Universal Precautions. ORG and PS shall inform all employees of ORG involved in the propagation of HepaRG Cells and/or use of the Products of the existence of this Agreement and of the rights and restrictions herein; economic provisions may be excluded at ORG’s discretion.

### ORG shall pay all correct invoice amounts within thirty (30) days of receipt of the invoice.

### INTELLECTUAL PROPERTY RIGHTS

## ORG agrees to take all reasonable and necessary steps to protect the INSERM Patents and Confidential Information of BI, which includes the Standard Operating Procedures provided by BI, and the information within them. ORG shall treat and respect BI and INSERM Intellectual Property as though it was ORG’s own, and shall promptly notify BI of any infringement thereof of which it becomes aware, whether by an employee or agent of ORG or someone else. ORG shall assist BI in its efforts to protect its rights and will provide all reasonably necessary assistance and cooperation by assisting BI to resolve any infringement, counterfeiting, or passing off about which ORG has information. Any award of damages by the Court or other authority shall inure to the benefit of BI, and ORG shall not be entitled to take or institute any enforcement action (either by way of informal protest, actions or proceedings) unless so authorized by BI.

BPI hereby declares and warrants being granted an exclusive license on the INSERM Patents. ORG acknowledges such declaration by BPI. Also ORG shall not at any time do or cause to be done any act or thing, directly and indirectly, contesting or in any way impairing any part of the BPI’s rights under the INSERM Patents. ORG agrees that it will not attempt to learn the formulation or contents of any of the HepaRG media, nor to attempt to reverse engineer either HepaRG cells or Media. ORG agrees that it will not represent that it has any ownership or interest in the INSERM Patents, BI License, or HepaRG Media except as expressly provided in this Agreement.

Notwithstanding anything to the contrary in this Agreement, all transfected material, all derived cell lines, and all animal models as the case may be (hereinafter “**New Material**”) developed as a result of the use of the Products under this Agreement shall be solely owned by ORG. PS shall promptly notify BI of the existence and nature of any such transfected material, cell lines, or animal models. PS and ORG will, upon written request by BI, promptly provide BI with samples of all the New Material and BPI will have the first option rights for commercial use on the IP generated by the ORG.

BI may itself produce or have produced on its behalf such New Material, with BI paying to ORG the reasonable cost to provide such samples to BI.

Any Invention using Products and made by PS and/or ORG that is considered under patent law to be an improvement of BI’s pre-existing rights, or that arises as a result of use of the Products **outside** of the rights provided in this Agreement, shall be the sole property of BI.

**WARRANTIES, INDEMNITY AND LIABILITY**

## The Parties each represent and warrant that it has legal power, authority and right to enter into this Agreement and to perform its respective obligations under this Agreement. The Parties each represents and warrants that at the Effective Date, it is not a party to any other agreement, arrangement or understanding with any third-party which prevents it from fulfilling any of its material obligations under this Agreement.

## The Parties each represent and warrant that the execution, delivery, and performance of this Agreement will not result in a breach or violation of, or constitute a default under, any statute, regulation, court order, or other law or agreement or instrument to which it is a party or by which it is bound.

### BI MAKES NO OTHER EXPRESS OR IMPLIED WARRANTIES WHATSOEVER AND SPECIFICALLY DISCLAIMS ANY AND ALL IMPLIED WARRANTIES, INCLUDING BUT NOT LIMITED TO, IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE, VALIDITY OF PATENT RIGHTS, NON-INFRINGEMENT, AND ANY IMPLIED WARRANTY ARISING FROM COURSE OF PERFORMANCE, COURSE OF DEALING, USAGE OF TRADE OR OTHERWISE.

### ORG hereby indemnifies and holds BI harmless from and against any and all claims, liabilities, losses, expenses, costs and damages whatsoever asserted by any third-party arising out of or in connection with the use of the Products by ORG or its employees, or with the use, handling, storage, manufacturing, sale or disposal of any Products or data derived from the HepaRG Cells and/or Media.

### CONSEQUENCES OF TERMINATION

Upon termination of this Agreement :

1. ORG shall cease using and, at BPI’s request, destroy or return to BI any HepaRG Cells and Media in ORG’s possession or control. In the case of any unused Media which has been properly stored and returned to BI in usable condition, BPI shall reimburse ORG for the amounts paid for such Media.
2. If BI instructs ORG to destroy HepaRG Cells, such destruction shall be attested to in written communication to BI by an individual other than PS, but of at least the same rank within ORG.
3. The sublicense rights granted by BI to ORG shall terminate immediately.
4. ORG shall pay to BI within thirty (30) days all sums due to BI which have accrued prior to the date of termination or expiry.

**WAIVER**

Neither Party shall be deemed to have waived any of its rights or remedies conferred by this Agreement, unless the waiver is made in writing and signed by a duly authorized representative of that Party. In particular, no delay or failure of either Party in exercising or enforcing any of its rights or remedies conferred by this Agreement shall operate as a waiver of those rights or remedies or so as to preclude or impair the exercise or enforcement of those rights or remedies, nor shall any partial exercise or enforcement of any right or remedy by either Party preclude or impair any other exercise or enforcement of that right or remedy by that Party.

**ENTIRE AGREEMENT/VARIATIONS**

This Agreement constitutes the entire agreement and understanding between the Parties and supersedes all prior oral or written understandings, arrangements, representations or agreements between them relating to the subject matter of this Agreement. No variation, amendments, modification, or supplement to this Agreement shall be valid, unless made in writing in the English language and signed by a duly authorized representative of each Party.

**NOTICES**

Any notices under this Agreement shall be in writing and in the English language. These notices shall be delivered by hand, sent by registered or recorded delivery airmail post to the address provided below, or alternatively, such other address as a Party may from time to time designate by written notice to the other Party.

**ASSIGNMENT**

Without the prior written consent of the other Party, neither Party shall assign the benefit and/or burden of this Agreement nor sub-contract any of its obligations under this Agreement, unless otherwise permitted by the terms of this Agreement. However, either Party may assign their rights and obligations to a third-party only if that third-party acquires, joins, merges with, or takes over the assigning Party.

**SEVERABILITY**

Should any part of this Agreement be declared illegal or unenforceable, the Parties will cooperate to obtain substantially the same result or as much as may be possible, including taking reasonably appropriate steps to amend, modify, or alter this Agreement.

If any term or provision of this Agreement shall be declared to be illegal by a final adjudication of any tribunal or court of competent jurisdiction, such adjudication shall not alter the validity or enforceability of any other Paragraphs, unless the Paragraphs declared (by either Party) shall be one expressly defined as a condition precedent or as of the essence of this Agreement, or comprising an integral part of, or inseparable from the remainder of this Agreement.

**GOVERNING LAW AND JURISDICTION**

This Agreement shall be governed by and construed and interpreted in accordance with the laws of France. English shall be the official language of this Agreement. The Parties agree that any dispute arising out of this Agreement, which cannot otherwise be settled between them, shall be submitted for arbitration or other alternative dispute resolution proceeding in France.

If any legal action or proceeding, including arbitration, relating to the performance or the enforcement of any Paragraph of this Agreement is brought against a Party, the prevailing Party shall be entitled to recover reasonable legal fees, costs, and disbursements, in addition to any other relief to which the prevailing party may be entitled.

**THIS AGREEMENT DOES NOT CONSTITUTE A PARTNERSHIP**

None of the Paragraphs in this Agreement shall be deemed to constitute a partnership between the Parties and no Party shall have any authority to bind any other Party in any way, except as provided in this Agreement.

This Agreement is executed by duly authorized representatives of the Parties:

**ORGANIZATION** **BIOPREDIC INTERNATIONAL**

## Principal Scientist :\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ By:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

## Date:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

## Other representative:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date :\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

## Name :\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

## Title :\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

## Date :\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Schedule 1**

**HepaRG® Media and Pricing**

ADD71x Growth Medium Supplement 425euros/btl

ADD72x Differentiation Medium Supplement 425euros/btl