From:	Howard, Kristina
To:	perrin@garlic.com <perrin@garlic.com>
	pvlarton@abr-inc.com <pvlarton@abr-inc.com>
Date:	9/27/2012 12:11:55 PM
Subject:	Application
Attachments:	HFT Application_HowardKE_August 2012.pdf
	ABR Research Stmt_KHoward_Aug_2012.pdf

Hi Perrin,

I am enclosing my signed application for tissues. I have received a copy of the contract that was completed and you should be prepaid for $12K of tissue purchases. For the accounting portion I will need to receive an invoice for each shipment so that I can account for the use of tissue with our accounting department. If additional information is needed to complete this process, please let me know. Once the application is approved, I would like to setup a schedule to start receiving the tissue.

Kind Regards,
Kristina

ADVANCED BIOSCIENCE RESOURCES, INC.

APPLICATION FOR THE ACQUISITION OF

HUMAN FETAL TISSUE FOR RESEARCH

All requests for human fetal tissue are reviewed for feasibility of procurement and preparation. When approved, an individual protocol will be developed for the procurement, preparation and delivery of tissue samples, based on the information provided in this application and any subsequent communication.

I. APPLICANT INFORMATION

NAME: __Dr. Kristina Howard_____
TITLE: _____
COMPANY: __FDA_____
ADDRESS: _(b) (6)._____
ADDRESS: _(b) (6)_____
CITY,ST,ZIP: _(b) (6)_____

PHONE #: (b) (6) _____
ALT. #: (b) (6) _____
FAX #: (b) (6) _____
EMAIL: _Kristina.Howard@fda.hhs.gov

BILLING INFORMATION **Please send invoice to:**
BILL TO: Prepaid (contract #HHSF223201211452P)
COMPANY: _FDA, Dr. Kristina Howard_____
ADDRESS: _(b) (6)._____
ADDRESS: (b) (6) Mailstop: _____
CITY,ST,ZIP: (b) (6)_

ACCOUNTING DEPT. PHONE #:_____

P.O. # (if required by your company):_____
P.O. # is not required to submit application

DELIVERY OPTIONS:

_____ Same Day: Commercial carrier, hand delivered
Maximizes cell viability (***geographical limits***)
__X_ Next Day: Pickup, delivery Mon-Sat daytime
Economical for fresh, frozen specimens

Applicant will be charged for delivery fees.

Applicant may designate preferred carrier:
Carrier Name: __Federal Express_____
Account #: _____

Credit Card #: _____
Name on CC: _____
Expiration Date: _____

SHIP TO: _Dr. Kristina Howard_____
_FDA_____
_(b) (6)_____
(b) (6) _____
_(b) (6)_____

Please indicate how you heard about ABR: __Use of ABR tissues in my previous position_____

II. HUMAN FETAL TISSUE

Tissue specimens requested: _____Fetal liver and thymus_____

Preferred gestational age (6-24 weeks): _____**16 – 24 weeks**_____
Quantity requested (number of specimens/week): _One set of tissue (thymus/liver) approx. twice monthly
Proposed starting date: ____October 2012_____

CONTAGIOUS DISEASE SCREENING: Availability of test results varies from 24 hours to 7 days after procurement. Applicant requires the following tests to be performed by ABR:

_X___ No testing required

_____ HIV
_____ HBSAG
_____ CMV
_____ HSV
_____ RPR
_____ HCV

OTHER_____
_____
_____

1516 Oak Street, Ste 303 / Alameda, California 94501 / (510) 865-5872 / Fax (510) 865-4090 / email: abr@abr-inc.com

III. PRESERVATION

ABR uses *BioWhittaker RPMI-1640 With L-Glutamine* for tissue preparation, preservation and shipment. Applicant may supply ABR with other media specific to research needs. Please indicate preference below.

PRESERVATION METHODS AVAILABLE:

___X__ Fresh; shipped on wet ice
_____ Passive freezing on dry ice; shipped on dry ice
_____ "Snap" freezing in LN2; shipped on dry ice

_____ Media provided by applicant
___X_ Media provided by ABR (RPMI)

IV. DONOR INFORMATION

CONSENT VERIFICATION: Consent for tissue donation is obtained prior to specimen procurement. The consent is extremely confidential in nature and shall not be communicated to the researcher.

SPECIFIC DONOR INFORMATION: Charts are routinely examined for patient medical histories. Please identify any specific information sought and indicate contraindications to specimen procurement:
_____Do not want to receive tissues from known HIV or Hepatitis positive mothers. Also prefer not to receive tissues that have a known chromosomal abnormality (e.g. Trisomy 21). _____

V. RESEARCH DATA

TITLE OF RESEARCH PROJECT: _Testing Biologic Drug Products for Product Quality and Safety __

ABR will provide tissue to researchers who provide information on current research funding, and a short summary of their research intent. **(Please attach a brief synopsis of the research project named above.)** Researchers must agree to use the tissue solely for research purposes and to acknowledge ABR in any publications resulting from the use of ABR provided tissue. Updates on research progress will be requested at six-month intervals. Researchers agree to publish the results of the research as promptly after the completion of the research as is reasonably possible without jeopardizing the sponsor's right to secure patents or copyrights necessary to protect its ownership or control of the results of the research. Researchers agree to inform ABR of the name of the publication and the date of the issue in which the results will be published. It is the intent of this requirement to make the results available to the general public through acceptable means of publication.

VI. SOURCE OF FUNDING

Please identify the primary source of funding for this project.

NIH _____ Other Federal or State Grants __X__ Foundation Grants _____ Other (specify) _____

If this application is approved by ABR, ABR shall provide services to the applicant in accordance with the terms and the other conditions on the reverse side, and the signature of the applicant shall constitute acceptance of all such terms and conditions by applicant. The entire agreement between ABR and applicant relating to the services provided by ABR is expressly set forth herein, and any modification of or addition thereto shall be of no force or effect unless it is in writing and signed on behalf of ABR by a duly authorized representative.

BY SIGNING BELOW, THE APPLICANT ACKNOWLEDGES HAVING READ THE TERMS AND CONDITIONS ON THE FOLLOWING PAGE AND AGREES TO SUCH TERMS AND CONDITIONS.

Kristina E. Howard Digitally signed by Kristina E. Howard DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2000568056, cn=Kristina E. Howard Date: 2012.09.27 12:05:04 -04'00'

_____ _____

SIGNATURE and TITLE of APPLICANT DATE

Please return to:

ADVANCED BIOSCIENCE RESOURCES, INC.
1516 OAK STREET, SUITE 303
ALAMEDA, CALIFORNIA 94501
Telephone: 510-865-5872
Fax: 510-865-4090
Email: abr@abr-inc.com

TERMS AND CONDITIONS OF SERVICES

1. Services.

1.1 During the term of this agreement, and pursuant to the terms and conditions hereinafter set forth, ABR will use its best efforts to provide services in connection with supplying researcher with the types of human tissues set forth in this application, as approved by ABR, suitable for researcher requirements and in the amounts requested based upon ongoing discussions between researcher and ABR pursuant to the information sent by ABR.

1.2 Researcher acknowledges and agrees that ABR will provide the following types of services:

1. Removing tissue.
2. Preserving and processing tissue to a form suitable to the researcher needs.
3. Seeking consent for tissue donations from appropriate individuals, obtaining validly executed consent forms, and maintaining records of such consents in accordance.
4. Obtaining, labeling, storing, and delivering samples of donor or other required serum, and maintaining a system for matching such samples to specific tissue donations.
5. Preserving tissue viability and cleanliness during removal, processing, preservation, storage and transportation.
6. Storing tissue and transporting it to researcher in accordance with section 5.

1.3 In the event that tissues of the type specified in the application become unavailable to ABR, such that ABR is unable to perform the contemplated services, ABR shall have no obligation to perform such services.

2. Representations and Warranties. ABR hereby represents and warrants to researcher that (i) ABR will make no payments to anyone for any tissue transferred in connection with this agreement, and (ii) ABR will verify for each tissue delivery that appropriate consent was obtained for use of such tissue and any associated serum samples, and that adequate records of such consent are maintained; provided, however, that the parties hereto acknowledge and agree that such consents are extremely confidential in nature and shall not, in any case, be communicated to researcher. Researcher hereby represents and warrants to ABR that (i) researcher will neither sell nor transfer for valuable consideration any tissue received through ABR to anyone, (ii) researcher will use the tissue only to satisfy its objectives, which are, as acknowledged and agreed hereto, [research and clinical use], (iii) researcher agrees to inform ABR of any changes in clinical or research use of specimens received from ABR, or in any specifications, constraints, etc. in a timely manner, and (iv) researcher understands the bio-hazardous nature of human tissue and agrees to take proper precautionary measures at all times when handling tissue specimen.

3. Terms. The terms of this agreement shall be for one (1) year, beginning from the date hereof, and terminating one (1) year thereafter, unless either of the parties hereto shall have given to the other thirty (30) days written notice of its intention to terminate this agreement, whereupon same shall terminate thirty (30) days after date of said notice.

In default of notice as aforesaid from either party hereto, this agreement shall continue for further successive terms of one (1) year thereafter and in default of thirty (30) days written notice before the end of an annual term by either of the parties of its intention not to renew, whereupon this agreement shall terminate at the end of said term.

4. Payments. Researcher agrees to pay to ABR a fee for costs incurred by ABR in providing services in connection with the acquisition of each sample of tissue requested by researcher, to be mutually agreed upon by ABR and researcher upon approval of this agreement by ABR.

5. Shipment services.

5.1 All shipments will be made as soon as possible after request has been received by ABR from researcher.

5.2 Researcher acknowledges that networks of tissue availability are neither permanent nor dependable, but rather they fluctuate. However, ABR shall use its best efforts to transfer the tissue in the amounts requested by researcher.

5.3 Shipment will be made in the best possible manner so as to preserve the quality of the tissues. It is understood that the fragility of human tissue is such that damage may occur during shipment. ABR will use its best efforts to comply with the handling and shipment protocols provided by researcher.

5.4 ABR will package the tissue appropriately and, if so requested by researcher, will insure the shipment. Researcher agrees to bear all costs associated with insurance and shipment of any tissue.

5.5 The risk of loss and damage of any tissue or organs shall pass immediately to researcher when the shipment of such tissue or organs is deposited with a carrier for transportation at the F.O.B. point.

6. Limitation of liability. ABR SHALL NOT BE RESPONSIBLE OR LIABLE UNDER ANY SECTION OF THIS AGREEMENT OR UNDER ANY CONTRACT, NEGLIGENCE, STRICT LIABILITY OR OTHER LEGAL OR EQUITABLE THEORY, FOR THE COST OF PROCUREMENT OF SUBSTITUTIVE SERVICES, OR ANY INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES INCLUDING, BUT NOT LIMITED TO LOSS OF REVENUES AND LOSS OF PROFITS. ANY LIABILITY OF ABR UNDER ANY THEORY WHATSOEVER WILL BE LIMITED EXCLUSIVELY TO THE PROVISION OF EQUIVALENT SERVICES BY ABR OR, IF UNENFORCEABLE, TO PAYMENT OF AN AMOUNT NOT GREATER THAN ANY AMOUNT ACTUALLY RECEIVED BY ABR FROM RESEARCHER ON ACCOUNT OF THIS AGREEMENT.

7. No warranties. It is understood that human tissue is by nature neither permanent nor dependable. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, ABR MAKES NO REPRESENTATION OF ANY KIND, EXPRESSED OR IMPLIED, INCLUDING ANY REPRESENTATION WITH RESPECT TO THE SAFETY, EFFICACY OR MERCHANTABILITY OR THE FITNESS FOR ANY PURPOSE WITH RESPECT TO THE TISSUE TRANSFERRED TO RESEARCHER IN CONNECTION WITH THIS AGREEMENT.

8. Indemnification. Researcher shall indemnify, defend and hold ABR harmless from and against all claims, causes of actions, suits, damages and costs arising out of, resulting from, or otherwise in respect of, the use of tissue transferred in connection with this agreement, except where such claims are the result of negligence of ABR, its employees, staff or agents to (i) comply with any governmental requirements, or (ii) adhere to the terms of this agreement.

9. General. This agreement shall be governed by and interpreted under the laws of the State of California, excluding rules of conflicts of law. This agreement may not be assigned by either party without the prior written consent of the other.

We will be using fetal liver and thymus to isolate CD34+ hematopoietic stem cells (HSC) and to implant fetal liver and thymus tissues into severely immune compromised mice (NSG, NRG, etc.). Additionally, the mice are transplanted with HSC isolated from the same donor tissue, resulting in a bone marrow/liver/thymus (BLT) humanized mouse. This procedure permits the full reconstitution of a human immune system in a mouse and will permit us to test biologic drug products in these mice.

Biologics provide unique and effective treatments for numerous human diseases and medical conditions. The efficacy of these therapeutics can be compromised by the patients' immune response to the drug resulting in antibody-mediated alteration of the biologics' activity or bioavailability. It is well established that high molecular weight structures, such as protein aggregates in biologic drug products, can enhance immunogenicity. They can be a result of the pharmaceutical manufacturing process, shipping or temperature stress. Other factors critical in determining the propensity to generate immune responses include the route of administration, dose, and frequency and duration of administration. Because each biologic is unique, it is not possible to predict, *a priori*, the *in vivo* consequences of different sizes, types or quantities of aggregates. Further, since the immune system of different species can distinguish orthologous proteins as foreign, the immunogenicity of biologics in humans cannot be assessed by testing these drug products in non-human species. The recent advent of "humanized" mice that recapitulate the human hematopoietic system permits direct *in vivo* testing of the human immunogenicity of biologics. Such studies are critical for developing scientifically sound approaches for evaluating and mitigating risk to product quality caused by aggregates and/or other components of biologics.