HEPALIFE TECHNOLOGIES INC
Form 8-K
May 26, 2004

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

May 26, 2004

Date of Report (Date of earliest event reported)

HEPALIFE TECHNOLOGIES, INC.

(Exact name of registrant as specified in its charter)

Florida

(State or other jurisdiction of incorporation)

000-29819

(Commission File Number)

58-2349413

(I.R.S. Employer Identification No.)

1628 West 1st Avenue, Suite 216, Vancouver, British Columbia, V6J 1G1

(Address of principal executive offices)

(800) 518-4879

(Registrant s telephone number, including area code)

ITEM 1. Changes in Control of Registrant.

None.

ITEM 2. Acquisition or Disposition of Assets.

None.

ITEM 3. Bankruptcy or Receivership.

None.

ITEM 4. Changes in Registrant s Certifying Accountant.

None.

ITEM 5. Other Events.

On May 24, 2004, HepaLife Technologies, Inc. agreed to extend its Cooperative Research and Development Agreement (CRADA) with the USDA s Agricultural Research Service (ARS) for an additional three years through September 30, 2007.

ARS will receive a total of $807,828.00 in funds, of which $153,600.00 has been paid, to study experimental culture conditions for the ARS-PICM-19 cell line, its derivative cell lines, or other pig epiblast-derived liver cell lines (as described under ARS patent #5,532,156, Hepatocyte Cell Line Derived from the Epiblast of Pig Blastocysts) so as to optimize their hepatocyte functions for use as an in vitro liver model, for their use in an artificial liver device, and for their use in the in vitro assay of metabolic, toxic, or carcinogenic responses. Specific project objectives are the following:

1)

Develop feeder-cell-independent and serum-free medium cell culture systems allowing the growth and differentiation of ARS-PICM-19 cells, or subclones or subpopulations of the ARS-PICM-19 cells, under defined conditions.

2)

Develop spheroid cultures of PICM-19 cells without STO feeder cells and testing of rotating cell culture system (RCCS) for production and maintenance of spheroids.

3)

Investigate effects of accessory cells obtained from pig liver on ARS-PICM-19 growth, differentiation, and metabolic function.

4)

Assay ARS-PICM-19 cells and spheroids for liver specific functions by measuring P450 activity, -glutamyltranspeptidase activity, urea production, and ammonia clearance.

5)

Assay ARS-PICM-19 liver specific protein synthesis and secretion by electrophoretic, immunochemical, or mass spectrophotometric techniques.

6)

Develop and test, by in vitro assay, flow-through bioreactors that enable the growth, differentiation, and maintenance of metabolic function of the ARS-PICM-19 cell line, or its derivative cell lines, over long term culture (1-3 months).

7)

Develop and test multi-well cell culture formats for the in vitro assay of the effects of various test compounds on the metabolism and viability of ARS-PICM-19-derived hepatocytes or bile ductules.

8)

Genetically engineer ARS-PICM-19 cells to create derivative cell lines containing gene reporter constructs, e.g., green fluorescent protein (GFP) based constructs, so that GFP expression is linked to various cell metabolic responses or stimulation of various cell signal transduction pathways.

9)

Develop cell transformation assay formats to demonstrate and enable the utilization of the ARS-PICM-19 cell line for the study of mutagenic or carcinogenic processes.

Hepalife Technologies will provide funds for the salary of one post-doctoral researcher, one support scientist, and one technician for a period of three years and funds for the associated laboratory supplies and professional activities involved with conducting the CRADA objectives under the following payment schedule:

(1)

$65,422.80 on or before August 1, 2004;

(2)

$65,422.80 on or before November 1, 2004;

(3)

$65,422.80 on or before February 1, 2005;

(4)

$65,422.80 on or before May 1, 2005;

(5)

$65,422.80 on or before August 1, 2005;

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$65,422.80 on or before November 1, 2005;

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$65,422.80 on or before February 1, 2006;

(8)

$65,422.80 on or before May 1, 2006;

(9)

$65,422.80 on or before August 1, 2006;

(10)

$65,422.80 on or before November 1, 2006

ITEM 6. Resignations of Registrant s Director s

None.

ITEM 7. Financial Statements and Exhibits.

The following exhibit is filed herewith:

Exhibit Number	Description
10.1	Amendment and extension of Cooperative Research Agreement with the United States Department of Agriculture

ITEM 8. Change in Fiscal Year.

None.

ITEM 9. Regulation FD Disclosure

None.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

HEPALIFE TECHNOLOGIES, INC.

/s/ Harmel S. Rayat

Harmel S. Rayat

Secretary/Treasurer, Director

Date: May 26, 2004

EXHIBIT 10.1

UNITED STATES DEPARTMENT OF AGRICULTURE	TYPE OF RESEARCH AGREEMENT
	Cooperative Research and Development Agreement
RESEARCH AGREEMENT	AGREEMENT NO. TYPE OF ACTION
	58-3K95-3-0967 Amendment No. 3
AGENCY (Name and Address)	PERIOD OF AGREEMENT
Agricultural Research Service	10/01/02 through 9/30/07
1400 Independence Avenue SW	FEDERAL OBLIGATION / CHANGE IN FEDERAL OBLIGATION
Washington, D.C. 20250-0302	$ 0

This Agreement is authorized by the Federal Technology Transfer Act, 15 USC 3710a, *et seq.,* and is governed by its terms.

Items	**Descriptions**
1. Technology Transfer Coordinator	Harry D. Danforth
2. Cooperator	Hepalife Technologies, Inc. Suite 216 - 1628 West 1st Ave, Vancouver, BC, V6J 1G1

	Tax ID #
3. Principal Investigator	Harmel Rayat, Director
4. USDA Laboratory	Growth Biology Laboratory
	10300 Baltimore Ave.
	Beltsville, MD 20705-2350
5. USDA Researcher (ADODR)	Neil Talbott, Thomas Caperna
6. National Program Leader & Area	First & Last Name of NPL
7. Accounting Code	X91-1265-356
8. Amount	$807,828.00 (total for 5 years)
9. Finance Office	Budget & Fiscal Office
	USDA-ARS-BA
	Bldg. 003, Room 306, BARC-West
	Beltsville, MD 20705-2350
10. Cris No.	1365-31000-087-01T
11. Title of Project	OPTIMIZATION OF THE ARS-PICM-19 CELL LINE FOR AN IN VITRO MODEL OF PIG LIVER FUNCTION AND APPLICATION TO AN EXTRACORPOREAL LIVER ASSIST DEVICE
12. Log #	22659

This Agreement is amended, as follows:

The duration of the Agreement is extended for three (3) years through September 30, 2007. ARS will receive a total of $807,828.00 in funds of which $153,600.00 has been paid. The Statement of Work and Clause 9 have been changed and are incorporated herein. The Title of Project has been changed. ALL OTHER TERMS AND CONDITIONS REMAIN THE SAME.

FOR THE UNITED STATES DEPARTEMENT OF AGRICULTURE

SIGNATURE	TYPED NAME	DATE
/s/ Richard Brenner	**RICHARD J. BRENNER**	**May 19, 2004**

Authorized Departmental Officer

FOR THE COOPERATOR

(Signature of person(s) authorized by the governing body of the COOPERATOR to incur contractual obligations)

SIGNATURE	TYPED NAME AND TITLE	DATE
/s/ Harmel Rayat	**HARMEL RAYAT**	**May 24, 2004**

OTT COVER FORM

Clause 9

9.1

HEPALIFE shall have the first option to prepare and prosecute patent or Plant Variety Protection Certificate applications, foreign and domestic, on Subject Inventions owned or co-owned by the U.S. Government, subject to the following conditions:

a.

All documents shall be submitted to ARS sufficiently in advance of filing to allow ARS a reasonable opportunity to review and make recommendations thereon;

b.

Copies of all correspondence from the U.S. Patent and Trademark Office or Plant Variety Protection Office and foreign equivalent offices shall be provided promptly to ARS;

c.

The following USDA personnel shall be given an associate power of attorney or be listed as an attorney of record:

Patent Advisor

Patent Attorney

Evelyn Rabin

John Fado

USDA-ARS-OTT

USDA-OGC Rm. 3311

5601 Sunnyside Avenue

South Agriculture Bldg.

Beltsville MD

Washington, D.C. 20250-1415

Registration Number

Registration No. 27876

Tel: 301-504-4781

Tel.: 202-720-2421

Fax: 301-504-5060

Fax: 202-720-8706

9.2

The act of preparing and/or filing documents, *per se*, shall not entitle HEPALIFE to any rights in such Inventions or the reimbursement of costs incident to patent prosecution.

9.3

ARS shall have the right at any time, at its sole discretion, concerning Inventions solely owned by the U.S. Government, to: (1) assume responsibility for prosecuting any such application; and (2) permit any application to become abandoned or issued patent/certificate to expire, subject to the provisions of any license agreement relating to the subject matter.

9.4

ARS agrees to provide HEPALIFE consultation and advice in the preparation, filing, and prosecution of patent or Plant Variety Protection Certificate applications on Subject Inventions.

STATEMENT OF WORK

A.

Introduction/Background

ARS has developed several in vitro model systems to investigate various aspects of hepatic gene expression and metabolic regulation. These systems encompass both established cell lines and primary liver cell cultures. One stem-like cell line, derived from porcine epiblast (embryonic) tissue is the ARS PICM-19 cell line (ARS patent #5,532,156), has been partially characterized and is a non-transformed immortal cell line that possesses many characteristics similar to that of intact liver parenchymal cells. ARS interests would be greatly enhanced by further characterization and improvements in the culture technology that would ultimately result in the cell line not requiring feeder cell support and growth in a completely serum-free defined medium. These advancements would facilitate our understanding of regulatory events in pig liver gene/proteome expression and in regulation of nutrient metabolism. Further, it has already been demonstrated that the unique hepatic characteristics of the ARS-PICM-19 cell line would have potential application for use in the production of a rescue device for human patients in liver failure (ARS patent # 5,866,420; Artificial Liver Device , granted to ARS on 2/2/1999). To date, the cellular components of artificial liver devices that are being tested by other institutions are based on freshly isolated porcine hepatocytes, human transformed tumor cells, or poorly defined stem-like cells prepared from fresh human adult liver tissue. It is widely recognized that the greatest hindrance to the development of a completely functional artificial liver rescue device is the lack of an appropriate defined cell line that will provide the functions of an intact liver. The primary interest of Hepalife is to explore the possibility that the ARS PICM-19 cell line is indeed the most appropriate cell line to use in such a device.

B.

Objective

The overall objective of the work is to optimize the patented ARS-PICM-19 cell line as an in vitro model of the pig liver. The first objective is to investigate and discover culture conditions for the ARS-PICM-19 cell line, or modifications of the ARS-PICM-19 cell line technology itself, that will optimize function, i.e., culture conditions or cell line modifications that will enable, as closely as possible, the reproduction of normal pig liver functions in an in vitro environment. Directly related to the first objective will be the second and third objectives. The second objective is adapting and applying the optimized ARS-PICM-19 cell line technology to the development of an extracorporeal liver assist device as described in patent #5,866,420. The third objective is to use the ARS-PICM-19 cell line in the development of in vitro assay formats for testing, a.) cell metabolism and toxicity responses, b.) hepatocyte and bile duct epithelium cell function responses, and c.) cell transformation responses, i.e., loss of normal differentiation.

C.

Approach and Methodology

ARS will study experimental culture conditions for the ARS-PICM-19 cell line, its derivative cell lines, or other pig epiblast-derived liver cell lines (as described under ARS patent #5,532,156, Hepatocyte Cell Line Derived from the Epiblast of Pig Blastocysts) so as to optimize their hepatocyte functions for use as an in vitro liver model, for their use

in an artificial liver device, and for their use in the in vitro assay of metabolic, toxic, or carcinogenic responses. Specific project objectives are the following:

1) Develop feeder-cell-independent and serum-free medium cell culture systems allowing the growth and differentiation of ARS-PICM-19 cells, or subclones or subpopulations of the ARS-PICM-19 cells, under defined conditions.

2) Develop spheroid cultures of PICM-19 cells without STO feeder cells and testing of rotating cell culture system (RCCS) for production and maintenance of spheroids.

3) Investigate effects of accessory cells obtained from pig liver on ARS-PICM-19 growth, differentiation, and metabolic function.

4) Assay ARS-PICM-19 cells and spheroids for liver specific functions by measuring P450 activity, -glutamyltranspeptidase activity, urea production, and ammonia clearance.

5) Assay ARS-PICM-19 liver specific protein synthesis and secretion by electrophoretic, immunochemical, or mass spectrophotometric techniques.

6) Develop and test, by in vitro assay, flow-through bioreactors that enable the growth, differentiation, and maintenance of metabolic function of the ARS-PICM-19 cell line, or its derivative cell lines, over long term culture (1-3 months).

7) Develop and test multi-well cell culture formats for the in vitro assay of the effects of

various test compounds on the metabolism and viability of ARS-PICM-19-derived hepatocytes or bile ductules.

8) Genetically engineer ARS-PICM-19 cells to create derivative cell lines containing gene reporter constructs, e.g., green fluorescent protein (GFP) based constructs, so that GFP expression is linked to various cell metabolic responses or stimulation of various cell signal transduction pathways.

9) Develop cell transformation assay formats to demonstrate and enable the utilization of the ARS-PICM-19 cell line for the study of mutagenic or carcinogenic processes.

Hepalife will provide funds for the salary of one post-doctoral researcher, one support scientist, and one technician for a period of three years and funds for the associated laboratory supplies and professional activities involved with conducting the CRADA objectives.

D.

ARS Responsibilities

1.

Conduct these portions of the research project or perform the following tasks:

a. Hire one post-doctoral research associate, one support scientist, and one technician for a 2-3 year period.

b. Provide laboratory and office space for the research associate.

c. Provide fully equipped cell culture laboratory and protein chemistry laboratory.

d. Provide experimental animals (pigs) and slaughter facilities.

e. Acquire specific laboratory equipment, e.g.., RCCS, and supplies to conduct the CRADA objectives.

f. Conduct research on the optimization of the ARS-PICM-19 cell line, or its derivative cell lines (or related pig epiblast-derived cell lines), as an in vitro pig liver cell model, and adapt the ARS-PICM-19 liver cell technology to an extracorporeal liver assist device and to in vitro formats for metabolic, toxicological, and carcinogenicity assay.

g. Prepare progress reports on project objectives.

h. Prepare and submit technical reports for publication.

2.

a. Provide access to 1850 square feet of laboratory space in Building 200, Rooms 13, 202, 204 and 212, at the Beltsville Agricultural Research Center for those Hepalife personnel assigned to this project.

b. Provide utilities, services, and general support to Hepalife's personnel, as needed and available.

E.

Hepalife s Responsibilities

1.

Perform these portions of the research effort:

a. Provide funds for one post-doctoral research associate, one support scientist, and one technician for a 2-3 year period.

b. Provide funds for project related laboratory equipment, supplies, and off site research services such as electron microscopy and bioreactor component manufacturing.

c. Provide funds for position advertisement and travel expenses for position interviews.

d. Provide funds for professional activities of research associate such as travel to meetings and project specific training activities.

e. Prepare and file patent applications.

2.

Pay a total of $807,828.00 to ARS for the 5-year life of the CRADA.

a.

The payment schedule for the funds which remain to be paid is:

(1)

$65,422.80 on or before August 1, 2004;

(2)

$65,422.80 on or before November 1, 2004;

(3)

$65,422.80 on or before February 1, 2005;

(4)

$65,422.80 on or before May 1, 2005;

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$65,422.80 on or before August 1, 2005;

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$65,422.80 on or before November 1, 2005;

(7)

$65,422.80 on or before February 1, 2006;

(8)

$65,422.80 on or before May 1, 2006;

(9)

$65,422.80 on or before August 1, 2006;

(10)

$65,422.80 on or before November 1, 2006;

Total: $654.228.00

Second year funding arrangements as negotiated in the original CRADA are superseded by this amendment. No additional funds are owed for Year 2.

b.

Make checks or money orders out to the "Agricultural Research Service," cite Agreement No. 58-3K95-3-0967 thereon, and send to:

USDA, ARS, BA, Budget and Fiscal Office

10300 Baltimore Ave.

Bldg. 003, Rm. 306, BARC-West

Beltsville, Maryland 20705-2350

3.

Hepalife may pay the travel and per diem of ARS scientific representatives traveling pursuant to this Agreement if such payment receives the prior approval of the appropriate ARS Area Director.

4.

Describe any personnel and/or equipment Hepalife will furnish ARS.

Hepalife will provide funds for the hiring and laboratory research support of a post-doctoral research associate.

F.

ARS & Hepalife s Joint or Mutual Responsibilities

1.

Perform these portions of the effort jointly:

a. Develop strategy for design of a support system matrix to grow and maintain established ARS-PICM-19, or its derivative cell lines, or related pig liver epiblast-derived cell lines.

b. Evaluate efficacy of ARS-PICM-19, its derivative cell lines, or related epiblast-derived pig liver cell lines, in an in vitro pig liver model system for potential use in an extracorporeal liver assist device and in the development and testing of in vitro formats for assaying metabolic, toxicological, and carcinogenic responses in pig hepatocytes and bile ductules.

SCHEDULE 3 ESTIMATED BUDGET

TOTAL YEARS

	ARS Receive	ARS In-House	Hepalife

	Funds for		In-House
A. Salaries and Wages	408,400.00	99,628.00	360,000.00
B. Equipment	28,025.00	200,000.00	33,000.00
C. Materials and Supplies	265,500.00		
D. Travel			
1. Domestic	14,000.00	8,000.00	80,000.00
2. Foreign			
E. Facilities		224,000.00	84,000.00
F. Other Direct Costs	11,126.00	105,144.00	
G. TOTAL DIRECT COSTS	727,051.00	636,722.00	557,000.00
H. Indirect Costs	80,777.00		
I. TOTAL COSTS . $	807,828.00	636,722.00	557,000.00

YEAR 1

	ARS Receive	ARS In-House	Hepalife
	Funds for		In-House
A. Salaries and Wages	75,000.00	23,200.00	72,000.00
B. Equipment	13,025.00	50,000.00	6,000.00
C. Materials and Supplies	45,500.00		
D. Travel			
1. Domestic	2,000.00	2,000.00	8,000.00
2. Foreign			
E. Facilities		56,000.00	12,000.00
F. Other Direct Costs	2,715.00	26,244.00	
G. TOTAL DIRECT COSTS	138,240.00	157,444.00	98,000.00
H. Indirect Costs	15,360.00		
I. TOTAL COSTS . $	153,600.00	157,444.00	98,000.00

Year 2

	ARS Receive Funds for	ARS In-House	Hepalife In-House
A. Salaries and Wages			
B. Equipment			
C. Materials and Supplies			
D. Travel			
1. Domestic			
2. Foreign			
E. Facilities			
F. Other Direct Costs			
G. TOTAL DIRECT COSTS			
H. Indirect Costs			
I. TOTAL COSTS . $	0.00	0.00	0.00

Year 3

	ARS Receive Funds for	ARS In-House	Hepalife In-House
A. Salaries and Wages	125,900.00	24,244.00	96,000.00
B. Equipment	5,000.00	50,000.00	9,000.00
C. Materials and Supplies	80,000.00		
D. Travel			
1. Domestic	4,000.00	2,000.00	24,000.00
2. Foreign			
E. Facilities		56,000.00	24,000.00
F. Other Direct Costs	2,800.00	26,300.00	
G. TOTAL DIRECT COSTS	217,700.00	158,544.00	153,000.00
H. Indirect Costs	24,187.00		
I. TOTAL COSTS . $	241,887.00	158,544.00	153,000.00

Year 4

	ARS Receive Funds for	ARS In-House	Hepalife In-House
A. Salaries and Wages	135,500.00	25,456.00	96,000.00
B. Equipment	5,000.00	50,000.00	9,000.00
C. Materials and Supplies	80,000.00		
D. Travel			
1. Domestic	4,000.00	2,000.00	24,000.00
2. Foreign			
E. Facilities		56,000.00	24,000.00
F. Other Direct Costs	2,800.00	26,300.00	
G. TOTAL DIRECT COSTS	225,300.00	159,756.00	153,000.00
H. Indirect Costs	25,030.00		
I. TOTAL COSTS . $	250,330.00	159,756.00	153,000.00

Year 5

	ARS Receive Funds for	ARS In-House	Hepalife In-House
A. Salaries and Wages	74,000.00	26,728.00	96,000.00
B. Equipment	5,000.00	50,000.00	9,000.00
C. Materials and Supplies	60,000.00		
D. Travel			
1. Domestic	4,000.00	2,000.00	24,000.00
2. Foreign			
E. Facilities		56,000.00	24,000.00
F. Other Direct Costs	2,811.00	26,300.00	

G. TOTAL DIRECT COSTS	145,800.00	161,028.00	153,000.00
H. Indirect Costs	16,200.00		
I. TOTAL COSTS . $	162,011.00	161,028.00	153,000.00