According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0579-0036. The time required to complete this information collection is estimated to average 2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data

needed, and completing and reviewing the collection of information.

OMB APPROVED Exp.: 10/31/2018

This report is required by law (7 U.S.C. 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

No 0180-DOA-AN

Fiscal Year 2016

UNITED STATES DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. REGISTRATION NUMBER

14-R-0192 (Customer Number: 23918)

2. HEADQUARTERS RESEARCH FACILITY (Name, address, and telephone number as registered with USDA. Include ZIP Code)

57 Union Street Worcester, MA 01608

Telephone: 508-459-7544

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets, if

FACILITY LOCATIONS (Sites)

Animals Covered By The Animal Welfare Regulations	B.  Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C.  Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	(Attach additional sheets, if necess  D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic analgesic, or tranquilizing drugs were used	E. Number of animals upon which teaching, experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress on these animals and the reasons such drugs were not used must be attached to this report.)	TOTAL NUMBER OF ANIMALS (Cols. C + D + E)
4. Dogs					0
5 Cats					0
6. Guinea Pigs		14	19	91	124
7. Hamsters		12	144		156
8 Rabbits			272		272
9. Non-human Primates			510	10	520
10. Sheep					0
11. Pigs					0
12 Other Farm Animals					
13. Other Animals					0
Cotton Rats		16			16
					0
					0

- Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility
- 2) Each principal investigator has considered alternatives to painful procedures
- This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator 3) and approved by the institutional Animal Care and Use Committee (IACUC) A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected
- The attending veterinarian for this research facility has appropriate authority to ensure the provisions of adequate veterinary care and to oversee the adequacy of other aspects of enimal care and 4.1

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(Chief Executive Officer (C.E.O.) or Legally Responsible Institutional Official (I.O.))

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

NAME AND TITLE OF C.E.O. OR I.O. (Type or Print) 0

DATE SIGNED

APHIS FORM 7023 JUL 2013

NP 1/2/18





File No. 23918/BRM/0215

December 13, 2017

United States Department of Agriculture, Animal Care Eastern Region 920 Main Campus Drive, Suite 200 Raleigh, NC 27606-5210

#### RE: Annual Report of Research Facility (APHIS Form 7023) Certificate Number 14-R-0192, Amendment to

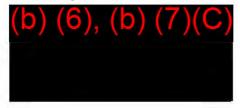
Dear Ms. / Sir.

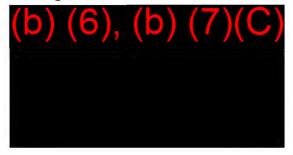
Please refer to our subject report for the current year submitted on November 17, 2017 which may please be discarded. Due to an oversight certain number of animals had not been included under column D of rows 6. The error is being corrected now by this submission.

Enclosed please find revised APHIS Form 7023 and Column E explanations for the reporting period October 01, 2016 – September 30, 2017 in respect of registration number: 14-R-0192.

The information excluding the above remains unchanged.

Sincerely,





ee:

Mark Nedelman, M.S. CEO, Biomere

#### Attachment (Item 6)

#### Column E Explanation Form

This form is intended as an aid to completing the Column E explanation. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

- 1. IACUC approved protocol number and date: 15-04, 2/2/15
- 2. Number of animals used under Column E conditions in this study: 91
- 3. Species (common name) of animals used in this study: guinea pig
- 4. Explain the procedure producing pain and/or distress, including reason(s) for species selected. (Cut/paste from the approved docket and or amendments).

Guinea pigs are the major animal infection model established for the human herpes virus-2 (HSV-2) to evaluate protective efficacy of potential HSV-2 vaccines and therapeutic test compounds. The Hartley guinea pig model was chosen to observe clinical signs, body weight and mortality post HSV-2 infection and treatment with potential therapeutic test substances. Post infection, animals were monitored daily for clinical signs of disease. The viral infection of guinea pigs with HSV-2 can have varying clinical readouts from no clinical signs to morbidity. To evaluate the viral disease, we followed the established published literature for viral clinical scoring listed in the table below. Animals that reached a moribund state or exhibited a score of (4) or a loss of 30% body weight were immediately euthanized humanely.

Observation	Score
No clinical signs of disease	0
Vaginal erythema	1
Single to a few modest herpetic lesions	2
Large or fused vesicles	3
Severe vaginal ulceration and paralysis	4
Found dead	5

# 5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Analgesics may interfere with immune responses and physiological processes of the infection and the display of disease symptoms and interfere or obscure immune protection results. The measurement of clinical scores is vital to the determination of the efficacy of the vaccine. Therefore, we did not use analgesics that could interfere with test results. For example, morphine is known to suppress the innate immune system and reduce severity of HSV-1 infection; the opioid derivative buprenorphine may have similar effects; the cyclooxegenase-2 (Cox-2) pathway is required for efficient herpes virus replication: NSAIDS down-regulate this pathway and Cox-2 inhibitors limit the replication of herpes viruses; Lidocaine destabilizes the HSV virion. Therefore, animals exhibiting pain or unrelieved distress (reached a moribund state or exhibit a score of 4) or a loss of 30% body weight were immediately euthanized.

Agency	None	CFR	

#### Attachment (Item 9)

#### Column E Explanation Form

This form is intended as an aid to completing the Column E explanation. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

- 1. IACUC approved protocol number and date: 15-16, approved 11/12/15
- 2. Number of animals used under Column E conditions in this study 10
- 3. Species (common name) of animals used in this study Callithrix jacchus (common marmoset)
- 4. Explain the procedure producing pain and/or distress, including reason(s) for species selected. (Cut/paste from the approved docket and or amendments). Experimental autoimmune encephalomyelitis (EAE) is induced by immunization of animals with human recombinant myelin oligodendrocyte glycoprotein (rhMOG) emulsified in complete Freund's adjuvant (CFA) once on Day 1 by intradermal injection to the back in 2 spots (50 100 μL/spot). After a variable latency period, animals will develop mild symptoms of EAE (altered vision and gait) followed by rapid progression, including partial to total limb paralysis. Onset of disease symptoms may be associated with pain and distress that was not alleviated to allow for end point analysis (evaluation of Test Article effects). Humane end points were used to minimize possible pain and distress. The marmoset has been published as a reliable NHP model for EAE allowing for efficacy testing of novel biologics that would not be possible to test in small animal species due to immune system cross-reactivity to the test article target and immunogenicity.
- 5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Experimental autoimmune encephalomyelitis (EAE) is an autoimmune disease model in which the immune system is triggered to attack a self-component. Treatment with Non-steroid anti-inflammatory drugs (NSAIDs) would alter this immune process and thus compromise the model and purpose of the study.

Agency	None	CFR	

#### 2016082568439766 Insp\_id

#### **Inspection Report**

Biomedical Research Models Inc	Customer ID:	23918
57-3 Union Street	Certificate:	14-R-0192
Worcester, MA 01608	Site:	001

Site: 001

BIOMEDICAL RESEARCH MODELS INC

Type: **ROUTINE INSPECTION** 

Date: 28-JUN-2017

There were no AWA regulated research activities at this site of the Registrant at the time of the inspection.

NOTE - Exit briefing held 6/29/17 on-site with facility representatives.

\*END OF REPORT\*

Prepared By: Date: GLADUE PAULA, V M D USDA, APHIS, Animal Care 29-JUN-2017

VETERINARY MEDICAL OFFICER 1054 Title:

Obtained by Rise for Animals. Uploaded 07/06/2020 Received By:

(b) (6), (b) (7)(C) **Title:** 19-04205 0000

Date: 29-JUN-2017



Customer: Inspection Date:

23918 28-JUN-17

# **Animal Inspected at Last Inspection**

Cust No	Cert No	Site	Site Name	Inspection
23918	14-R-0192	001	BIOMEDICAL RESEARCH	28-JUN-17
No Anima	als were Inspect	ed.	MODELS INC	
Count	Species			
000000	NONE			
000000	Total			

#### 2016082568439796 Insp\_id

#### **Inspection Report**

Biomedical Research Models Inc 57-3 Union Street Worcester, MA 01608	Customer ID: Certificate: Site:	23918 14-R-0192 003 DICAL RESEARCH MODELS INC
	Type: Date:	ROUTINE INSPECTION 28-JUN-2017
There were no non-compliant items identified	during the inspection.	
NOTE - Inspection conducted 6/28/17 and 6/2	9/17. Exit briefing held 6/29/17	on-site with facility representatives.
*END OF REPORT*		
Prepared By:		
GLADUE PAULA, V M D	USDA, APHIS, Animal Care	— <b>Date:</b> 29-JUN-2017

Title: VETERINARY MEDICAL OFFICER 1054

Received By: Obtained by Rise for Animals. Uploaded 07/06/2020

(b) (6), (b) (7)(C)

**Title:** 19-04205\_00000

(b) (6), (b) (7)(C)

**Date:** 29-JUN-2017



United States Department of Agriculture Customer: 23918

Animal and Plant Health Inspection Service Inspection Date: 28-JUN-17

# **Animal Inspected at Last Inspection**

Cust No	Cert No	Site	Site Name	Inspection
23918	14-R-0192	003	BIOMEDICAL RESEARCH MODELS INC	28-JUN-17
Count	Species			
000014	RHESUS MACAQU	JE		
000015	DOMESTIC RABBI	T / EURO	PEAN RABBIT	
000298	CRAB-EATING MA	CAQUE /	LONG-TAILED MACAQUE / CYNOMOLGUS MONKEY	
000327	Total			



### **Teachable Moments**

Legal Name:	BIOMEDICAL RESEARCH MODELS INC			
Customer Numl	per:	Certificate Numb	per:14-R-0192	
Inspection Date: 28-JUN-17		Site Number: _	003	
Inspector:	PAULA GLADUE, V M D			
Section:				
Occion.				

#### 3.80(a)(2)(ii) PRIMARY ENCLOSURES.

Flexible water lines to the lixits need to be modified to prevent access to the lines by the NHPs.



2016082569224882 Insp\_id

#### **Inspection Report**

Biomedical Research Models Inc	Customer ID:	23918
57-3 Union Street	Certificate:	14-R-0192
Worcester, MA 01608	Site:	003

BIOMEDICAL RESEARCH MODELS INC

Type: ROUTINE INSPECTION

Date: 24-JUL-2018

There were no non-compliant items identified during the inspection.

NOTE - Inspection conducted 7/24/18 and 7/25/18. Exit briefing held 7/25/18 on-site with facility representatives.

\*END OF REPORT\*

Prepared By:

GLADUE PAULA, V M D USDA, APHIS, Animal Care

Date: 25-JUL-2018

Title: VETERINARY MEDICAL OFFICER 1054

Received By: Obtained by Rise for Animals. Uploaded 07/06/2020

(b) (6), (b) (7)(C)

Date:

25-JUL-2018



Customer: 23918 Inspection Date: 24-JUL-18

# **Species Inspected**

Cust No	Cert No	Site	Site Name	Inspection
23918	14-R-0192	003	BIOMEDICAL RESEARCH MODELS INC	24-JUL-18
Count	Scientific Name		Common Name	
000323	Macaca fascicularis	S	CRAB-EATING MACAQUE / CYNO	OMOLGUS MONKEY
000028	Macaca mulatta		RHESUS MACAQUE	
000053	Oryctolagus cunicu	ılus	DOMESTIC RABBIT / EUROPEAN	I RABBIT
000404	Total			



#### **Teachable Moments**

Legal Name:	BIOMEDICAL RESEARCH MODELS INC	;	
Customer Numb	per:	Certificate Number:	14-R-0192
Inspection Date	24-JUL-18	Site Number:	003
Inspector:	PAULA GLADUE, V M D		
Section:			

#### 2.31(d)(5) INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

The IACUC shall conduct continuing reviews of ongoing activities involving animals at appropriate intervals as determined by the IACUC, but the continuing reviews shall not be conducted less than annually.



2016082569487110 Insp\_id

Inspection Report			
Biomedical Res 57-3 Union Stre Worcester, MA		Customer ID: Certificate: Site:	<b>23918 14-R-0192</b> 001
			DICAL RESEARCH MODELS INC
		Type: Date:	FOCUSED INSPECTION 16-MAY-2019
There were no a	AWA regulated research activities	s at this site of the Registrant	t at the time of the inspection.
NOTE - Exit bri	efing held 5/16/19 on-site with fac	cility representatives. Report	delivered by email 5/16/19.
*END OF REPO	DRT*		
Prepared By:			
Title:	GLADUE PAULA, V M D U	ISDA, APHIS, Animal Care	— <b>Date:</b> 16-MAY-2019
Received By:			by Rise for Animals. Uploaded 07/06

Date: 16-MAY-2019



Customer: 23918 Inspection Date: 16-MAY-19

# **Species Inspected**

Cust No	Cert No	Site	Site Name	Inspection
23918	14-R-0192	001	BIOMEDICAL RESEARCH MODELS INC	16-MAY-19

No Animals were Inspected.

 Count
 Scientific Name
 Common Name

 000000
 NONE
 NONE

000000 Total



2016082569487123 Insp\_id

#### **Inspection Report**

Biomedical Res 57-3 Union Stre Worcester, MA		Customer ID: Certificate: Site:	14-R-0192
		Type: Date:	FOCUSED INSPECTION 16-MAY-2019
There were no	non-compliant items identified du	ring the inspection.	
NOTE - Exit bri	efing held 5/16/19 on-site with fac	cility representatives. Report	delivered by e-mail 5/16/19.
*END OF REPO	ORT*		
Prepared By:			- Date:
Title:	GLADUE PAULA, V M D UVETERINARY MEDICAL OFFI	JSDA, APHIS, Animal Care CER 1054	16-MAY-2019
Received By:		Obtained	by Rise for Animals. Uploaded 07/06/

Date:



Customer: 23918 Inspection Date: 16-MAY-19

# **Species Inspected**

Cust No	Cert No	Site	Site Name	Inspection
23918	14-R-0192	003	BIOMEDICAL RESEARCH MODELS INC	16-MAY-19
Count	Scientific Name		Common Name	
000262	Macaca fascicularis CRAB-EATING MACAQUE / CYNOMOLGUS MONKEY		NOMOLGUS MONKEY	
000063	Macaca mulatta		RHESUS MACAQUE	
000038	Oryctolagus cunicu	lus	DOMESTIC RABBIT / EUROPEA	N RABBIT
000363	Total			

# Research Facility Protocol Selection Worksheet

Legal Name: Biomedical Research Models Inc

Customer Number: 23918 Certificate Number: 14-R-0192 Site Number: 001 & 003

Inspection Date: 5/16/19

Inspection Type: Routine Focused (list areas inspected)

Animals and Animal Housing; Produce storage; IACUC minutes; Reports to IO; FY 18 USDA AR; 2 protocols

Inspector: PSGladue, VMD

Reason	s Protocols Were Selected for Review :	How Many Protocols Were Selected	
1.	Protocols identified during inspection of concern (select all)	0	
2.	Column E protocols ( select all)	0	
3.	Protocols with IACUC-approved exemptions/exceptions (select all)	0	
4.	Protocols cited as noncompliant and not corrected during the last inspection (select all)	0	
5.	Additional Protocols Selected:	2	
	<ul> <li>a. If &lt;5 remaining protocols, select all remaining:</li> <li>b. If &gt;5 remaining protocols, select 5 additional protocols:</li> <li>1) Protocol for each regulated species and/or,</li> <li>2) Protocols involving high risk procedures (see Chapter 7, Animal Welfare Inspection Guide for guidance):</li> </ul>		
То	tal Protocols Selected and Reviewed	2	

<sup>\*</sup>Note: Protocol selection guidance applies to protocols which have been initially approved, or have had significant changes approved, since the last inspection. For protocols reviewed by an Animal Care Veterinary Medical Officer within the last year, professional judgment should be used in determining whether another review is necessary.

Version 2/11/19

From: (b) (6), (b) (7)(C)

To: Gladue, Paula S - APHIS

Subject: RE: \*\*\*Action required - USDA inspection reports BRM 001 5/16/19 focused & BRM 003 5/16/19 focused

**Date:** Friday, May 17, 2019 7:45:09 AM

Hi Paula,

I received the inspection reports. Thanks and have a great weekend



From: Gladue, Paula S - APHIS <paula.s.gladue@usda.gov>

**Sent:** Thursday, May 16, 2019 8:50 PM

**To:** (b) (6), (b) (7)(C) < (6) (6), (6) (7)(C) @biomere.com>

Subject: \*\*\*Action required - USDA inspection reports BRM 001 5/16/19 focused & BRM 003

5/16/19 focused **Importance:** High



Here are the inspection and inventory reports from the inspection conducted Thursday 5/16/19 plus the Research Protocol Selection form. Please note that if you are viewing this e-mail on an iPhone that the RPS form may appear blank but is filled out when viewing it on a computer.

I have sent the reports in a PDF format. \*\*\*Please acknowledge within 5 days that you successfully received the inspection reports via a return e-mail to me.\*\*\* The return e-mail takes the place of a "received by" signature on the reports.

If you are having any difficulty sending an e-mail response, please let me know by calling me at 860-423-6431 and I can send the reports to you by a different method.

Thanks and enjoy the upcoming finally dry weekend!

Paula

Paula S. Gladue, V.M.D. USDA/APHIS/Animal Care P.O. Box 117; Willimantic; CT 06226 Office (860) 423-6431

This electronic message contains information generated by the USDA solely for the intended recipients. Any unauthorized interception of this message or the use or disclosure of the information it contains may violate the law and subject the violator to civil or criminal penalties. If you believe you have received this message in error, please notify the sender and delete the email immediately.



Mullion Street, Worcester, MA 01608 508 459 7544biomere.com

OCT 0 2 2017

File No. 23918/BRM/0215

September 27, 2017

14-R-0192

Elizabeth Goldentyer, D.V.M. Regional Director- USDA, APHIS, Animal Care Eastern Region 920 Main Campus Drive, Suite 200 Raleigh, NC 27606-5213

RE: Customer ID number: 23918. Change in IACUC Members effective September 22, 2017

Dear Dr. Goldentyer:

This letter is to inform you of changes to our IACUC Roster.

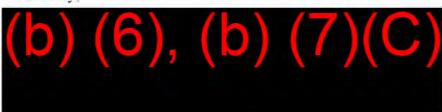
(b) (6), (b) (7)(C) is no longer a member of the Biomere IACUC effective as of September 22, 2017.

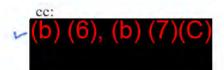
(b) (6), (b) (7)(C) has resigned from the Biomere IACUC effective as of October 2, 2017.

(b) (6), (b) (7)(C) has been appointed as a member of the Biomere IACUC effective October 2, 2017. has 20 years' experience working with laboratory rodent models.

This change in the program will be reflected in the 2017 Annual Report.

Sincerely,





∠(b) (6), (b) (7)(C)





File No. 23918/BRM/0215

May 23, 2019

United States Department of Agriculture, Animal Care Eastern Region 920 Main Campus Drive, Suite 200 Raleigh, NC 27606-5210

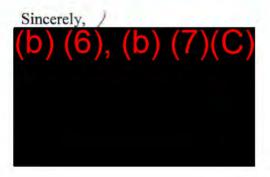
RE: IACUC Member Updates effective May 23, 2019: Certificate Number 14-R-0192.

This letter is to inform you of changes to Biomere's IACUC Roster.

(b) (6), (b) (7)(C) has been appointed to Biomere's IACUC as a non-affiliated active member for IACUC effective as of May 23, 2019. (b) (6), (b) (7)(C) has served on Biomere's IACUC as the non-affiliated stand-by member for the last 2 years'.

(b) (6), (b) (7)(C) has resigned as IACUC's non-affiliated active member for Biomere effective as of May 23, 2019.

This change in the program will be reflected in the 2019 Annual Report.







JUN 1 4 2017

File No. 23918/BRM/0215

June 13, 2017

Elizabeth Goldentyer, D.V.M. Regional Director- USDA, APHIS, Animal Care Eastern Region 920 Main Campus Drive, Suite 200 Raleigh, NC 27606-5213

RE: Customer ID number: 23918. (b) (7)(F) 57 Union Street, Worcester, MA Facility effective June 15, 2017

Dear Dr. Goldentyer:

This letter is to inform you of the opening of an additional floor of Biomere's 57 Union Street, Worcester, MA facility.

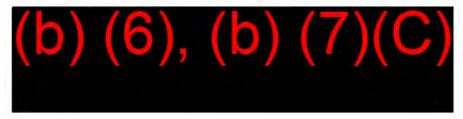
(b) (7)(F)

The city of Worcester approved an occupancy permit for the area effective June 13, 2017. This brings the total occupied space to

(b) (7)(F)

This change in the program will be reflected in the 2017 Annual Report.

Sincerely.



(b) (6), (b) (7)(C)

(b) (6), (b) (7)(C)