Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Tuesday, September 01, 2009 3:38 PM
To: Berkley, Dale (NIH/OD) [E]; Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: FW: MTA for reverse genetics plasmids
Attachments: NCIRD-V095251-00 StJude 01Sept09.doc

Here is the response from the program. It appears that they will not be using the plasmid set for any prohibited reason. Therefore, I will go ahead and try to execute the agreement as it appears in the attached.

Thanks again for all your help.

Janice

From: Gubareva, Larisa (CDC/CCID/NCIRD)
Sent: Tuesday, September 01, 2009 3:06 PM
To: Knight, Janice (CDC/CCID/OD); Klimov, Alexander (CDC/CCID/NCIRD)
Cc: Hoelscher, Mary (CDC/CCID/NCIRD); Gubareva, Larisa (CDC/CCID/NCIRD)
Subject: RE: MTA for reverse genetics plasmids

Janice,
I have no problem with restrictions. We intent to use this system only for our laboratory research needs.
Thank you very much,
Larisa

From: Knight, Janice (CDC/CCID/OD)
Sent: Tuesday, September 01, 2009 2:41 PM
To: Klimov, Alexander (CDC/CCID/NCIRD); Gubareva, Larisa (CDC/CCID/NCIRD)
Cc: Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: FW: MTA for reverse genetics plasmids
Importance: High

Sasha, Larisa,

Please note the following restrictions as per email from Dale Berkley NIH/OD on your use of the St. Jude plasmid set:

NIH

Do you have any intention of using the materials for either purposed stated above? I will wait on processing the reverse MTA until I get confirmation from you.

Best regards,

Janice

NIH

NIH

From: Knight, Janice C. (CDC)
Sent: Thursday, August 27, 2009 1:16 PM
To: Foster, Joseph A. (CDC); Berkley, Dale (NIH/OD) [E]
Cc: Blake-Dispigna, Lisa (CDC); Watkins, Andrew C. (CDC)
Subject: RE: MTA for reverse genetics plasmids

Joe, Dale,

In light of Andrew's comment, could you give me any recommendations on whether we can sign the MTA with St Jude? As I understand it the plasmid set to be provided has a different backbone to the earlier plasmids that Ruben Donis has.

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, August 27, 2009 9:48 AM
To: Foster, Joseph A. (CDC/OCOO/OD); Berkley, Dale (NIH/OD) [E]
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Knight, Janice (CDC/CCID/OD)
Subject: RE: MTA for reverse genetics plasmids

Given the previous sensitivities to this issue, I defer to OGC for their expert advice.

Andrew

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, August 26, 2009 4:59 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: FW: MTA for reverse genetics plasmids

Andrew,

The following appears in the attached proposed reverse MTA with St. Jude:

"*The Recipient acknowledges that the Materials and/or their method of production are or may be the subject of one or more patents or patent applications. Except as provided in this Agreement, no express or implied licenses or other rights are provided to the Recipient under any patents, patent applications, trade secrets or other proprietary rights of St. Jude. Recipient acknowledges no right or license is being granted by St. Jude under this MTA to commercialize or sell the Materials under any third party patents or patent applications or otherwise. To the extent any such rights or licenses are required, Recipient acknowledges that it is its responsibility to obtain such rights or licenses, as necessary. Recipient covenants that it will not use the Materials for commercial purposes such as screening, production or sale (including for any stockpile that is financially recognized by Recipient as revenue), without obtaining the necessary commercialization rights or licenses with respect thereto from (a)* (b)(4) *and its affiliates (or their respective successors), as holders of exclusive licenses of patents and/or patent applications of the reverse genetics methodology and/or products obtained using reverse genetics methods, and (b) any third parties that may have applicable rights in the Materials (or any materials used to produce Materials). Recipient acknowledges that certain restrictions set forth in this MTA are for the benefit of MedImmune, Inc. and that MedImmune, Inc. shall be deemed to be a third-party beneficiary to this MTA with the right of enforcement.*"

As you may remember we included very similar language in our earlier 2007 MTAs for distribution of influenza RG reassortants:

"*Recipient covenants that it will not use the Research Material for commercial purposes such as screening, production or sale (including for any stockpile that is financially recognized by Recipient as revenue), without obtaining the necessary commercialization rights or licenses with respect thereto from (a)* (b)(4) *and its affiliates (or their respective successors), as holders or exclusive licensees of patents and/or patent applications of the reverse genetics methodology and/or products obtained using reverse genetics methods, and (b) any third parties that may have applicable rights in the Research Material (or any materials used to produce the Research Material). Recipient agrees to comply with all Federal and/or National rules and regulations applicable to the Research Project and the handling of the Research Material. Recipient acknowledges that certain restrictions set forth in this MTA are for the benefit of MedImmune, Inc. and that MedImmune, Inc. shall be deemed to be a third-party beneficiary to this MTA with the right of enforcement. At the time of execution, the CDC laboratory distributing the technology and the CDC Technology Transfer Office have no knowledge of additional third party rights in the Research Material transferred by this Agreement.*" We removed this language from those MTAs as you felt we had given MedImmune enough "free advertisement" and just used the standard MTA language. Now it appears, we aren't using any legal documentation for influenza RG reassortant transfers.

So, my question: Can we sign St. Jude's MTA with as it appears above? This MTA is for RG plasmids not reassortants if that makes a difference.

Janice

From: Allay, Esther [mailto:Esther.Allay@STJUDE.ORG]
Sent: Friday, August 21, 2009 10:57 AM
To: Knight, Janice (CDC/CCID/OD)
Subject: FW: MTA for reverse genetics plasmids

Hi Janice:

I just spoke with MedImmune - they were wondering why the language in section 1 was struck. They are willing to consider this, but need an explanation before they can determine whether or not it will be acceptable. This same language is in the CDC's outgoing MTAs we have received for materials made using reverse genetics, so I'm not sure why CDC cannot agree in this MTA.

Regards,
Esther

From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
Sent: Wednesday, August 12, 2009 1:42 PM
To: Allay, Esther
Cc: Gubareva, Larisa (CDC/CCID/NCIRD)
Subject: RE: MTA for reverse genetics plasmids

Esther,

After discussions here, it is proposed the we use the version dated 12Aug09 I have attached above for this transfer. If you need to consult with (b)(4) then we will have to work within the delay.

Thanks so much,

Janice

From: Allay, Esther [mailto:Esther.Allay@STJUDE.ORG]
Sent: Tuesday, August 11, 2009 1:40 PM
To: Knight, Janice (CDC/CCID/OD)
Subject: FW: MTA for reverse genetics plasmids

Hi Janice:

Please see our comments in the attached. If you need "unmodified" in there, we will need to check with (b)(4) which may cause significant delays in executing the agreement.

Regards,
Esther

Esther R. Allay
Licensing Associate
Office of Technology Licensing - Mail Stop 742
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Phone: 901-595-4700
FAX: 901-595-3148
email: esther.allay@stjude.org <mailto:esther.allay@stjude.org>
www.stjude.org/technology-licensing

From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
Sent: Tuesday, August 11, 2009 7:52 AM
To: Allay, Esther
Cc: Gubareva, Larisa (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA for reverse genetics plasmids

Good morning Esther,

So nice to be working with you again. I apologize for the lengthy delay in responding to Dr. Gubareva's submission of the MTA, but I do hope we can move this quickly forward. I have attached your original agreement along with a revised document for your review containing a few minor changes to the template that I hope will be acceptable based on the previous MTA we executed in 2007.

Best regards,

Janice

From: Gubareva, Larisa (CDC/CCID/NCIRD)
Sent: Tuesday, March 24, 2009 2:59 PM
To: Knight, Janice (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD); Gubareva, Larisa (CDC/CCID/NCIRD); 'Esther.Allay@stjude.org'
Subject: FW: MTA for reverse genetics plasmids
Importance: High

Hello Janice,

Could you please review the terms in the attached MTA?
Please let us know if you have any questions.

Best regards,

Larisa

From: Allay, Esther [mailto:Esther.Allay@STJUDE.ORG]
Sent: Tuesday, March 24, 2009 2:05 PM
To: Gubareva, Larisa (CDC/CCID/NCIRD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD)
Subject: MTA for reverse genetics plasmids
Importance: Low

Dear Dr. Gubareva:

Dr. Richard Webby has forwarded to me your request for the above-cited materials. St. Jude Children's Research Hospital and Dr. Webby would be pleased to provide these materials to you and the CDC under the terms of the attached Material Transfer Agreement (MTA). Whereas the terms of the MTA are designed to have minimal effect on the progress of your research, any requests to revise the terms may significantly delay completion of the MTA.

Please print out two copies of the attached MTA, sign both copies and have an authorized official of the CDC sign both. Forward both copies to me at the address below. I shall return one fully executed original to you for your files.

To expedite the transfer of materials, you may fax (901-595-3148) a copy of the signed MTA back to me provided one with original signatures follows by mail. If you have any questions, you may contact me by phone (901-595-4700) or by e-mail at: esther.allay@stjude.org.

Regards,

Esther

Esther R. Allay
Licensing Associate
Office of Technology Licensing - Mail Stop 742
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Phone: 901-595-4700
FAX: 901-595-3148
email: esther.allay@stjude.org <mailto:esther.allay@stjude.org>
www.stjude.org/technology-licensing

Attachment

CDC Reference: NCIRD-V095251-00

March 24, 2009

Materials Transfer Agreement

Dr. Larisa Gubareva
Influenza Division
Centers for Disease Control and Prevention
1600 Clifton Road, NE
Atlanta, GA 30333

Dear Dr. Gubareva:

St. Jude Children's Research Hospital, Inc., ("St. Jude") agrees to provide Dr. Larisa Gubareva and the Centers for Disease Control and Prevention (collectively referred to herein as "Recipient") with materials developed at St. Jude by Drs. Erich Hoffmann and Robert Webster subject to the following terms and conditions of this Materials Transfer Agreement (this "Agreement" or "MTA"):

1. The biological materials to be provided to Recipient are:

   plasmids listed in Appendix A,

   including any progeny, portions, unmodified derivatives and any accompanying know-how or data ("Materials"). The Recipient acknowledges that the Materials and/or their method of production are or may be the subject of one or more patents or patent applications. Except as provided in this Agreement, no express or implied licenses or other rights are provided to the Recipient under any patents, patent applications, trade secrets or other proprietary rights of St. Jude. Recipient acknowledges no right or license is being granted by St. Jude under this MTA to commercialize or sell the Materials under any third party patents or patent applications or otherwise. To the extent any such rights or licenses are required, Recipient acknowledges that it is its responsibility to obtain such rights or licenses, as necessary. Recipient covenants that it will not use the Materials for commercial purposes such as screening, production or sale (including for any stockpile that is financially recognized by Recipient as revenue)., without obtaining the necessary commercialization rights or licenses with respect thereto from (a) (b)(4) Inc. and its affiliates (or their respective successors), as holders of exclusive licenses of patents and/or patent applications of the reverse genetics methodology and/or products obtained

using reverse genetics methods, and (b) any third parties that may have applicable rights in the Materials (or any materials used to produce Materials). Recipient acknowledges that certain restrictions set forth in this MTA are for the benefit of MedImmune, Inc. and that MedImmune, Inc. shall be deemed to be a third-party beneficiary to this MTA with the right of enforcement.

2. Upon receipt of Materials from St. Jude, Recipient accepts sole responsibility for any and all receipt, storage, handling, disposition, transfer and uses of the Materials. The Materials will be used exclusively for non-clinical, non-commercial research by Recipient, and will not under any circumstances be used in humans or in any process used to make a product intended for use in humans. Use will be in compliance with all applicable laws and regulations. St. Jude reserves the right to terminate this agreement immediately at any time upon thirty (30) days prior written notice to Recipient. Upon termination of this agreement, Recipient shall destroy all unused Materials.

3. The Materials will not be transferred, distributed or released to any third party unless prior written permission is obtained from St. Jude. Without limiting the foregoing, Recipient acknowledges and agrees that (i) the Materials may not be taken or sent to another institution or company without written permission from St. Jude and (ii) the Materials may not be used in research that is subject to consulting or licensing obligations to another party (other than those obligations imposed upon grantee institutions of the U.S. government) without express written consent by St. Jude. Recipient, its affiliates, agents and subcontractors agree to comply with all U.S. export control laws, rules and regulations with respect to its use and any permitted distribution of the Materials.

4. Recipient agrees to provide St. Jude with a copy of any publication that contains experimental results obtained from the use of the Materials, and will acknowledge St. Jude as the source of the Materials.

5. Recipient acknowledges St. Jude's ownership of the Materials and any progeny thereof. Recipient shall not commercialize any product that contains Materials without the prior written approval of St. Jude. The Recipient is free to file patent application(s) claiming inventions made by Recipient through use of the Materials but agrees to notify St. Jude within sixty (60) days of filing any patent application which claims subject matter that contains or incorporates the Materials or which claims a method of manufacture or use of the Materials.

6. The Materials provided are experimental in nature, and are provided WITHOUT ANY WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR USE. ST. JUDE MAKES NO

REPRESENTATION AND PROVIDES NO WARRANTY THAT THE USE OF THE MATERIALS WILL NOT INFRINGE ANY PATENT OR OTHER PROPRIETARY RIGHT. IN NO EVENT SHALL ST. JUDE BE LIABLE FOR ANY INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES, EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

7. No indemnification for any loss, claim, damage, or liability is intended or provided by either party hereto under this Agreement. Each party shall be liable for any loss, claim, damage or liability that said party incurs as a result of said party's activities under this Agreement except that Recipient, as an agency of the United States government, assumes liability only to the extent provided under the Federal Tort Claims Act (28 USC Chapter 171).

If the terms and conditions set forth above are acceptable, please return one copy to the Office of Technology Licensing after it has been signed by you and by an authorized official of your institution, and retain the other copy for your files. The Materials will be forwarded to you upon receipt of this signed Agreement.

ST. JUDE CHILDREN'S RESEARCH HOSPITAL, INC

By: _____

J. Scott Elmer
Director, Technology Licensing

Date: _____

CENTERS FOR DISEASE CONTROL and PREVENTION

By: _____

Melinda Wharton, MD MPH
Acting Director,
National Center for Immunization and Respiratory Diseases

Date: _____

RECIPIENT INVESTIGATOR

By: _____
Larisa Gubareva, MD PhD

Title: Senior Service Fellow

Date: _____

CDC Reference: NCIRD-V095251-00

APPENDIX A

List of reagents covered as "Materials" in MTA between St. Jude and the Centers for Disease Control and Prevention on behalf of Dr. Larisa Gubareva

pHW2000, the cloning vector

pHW181-PB2
pHW182-PB1
pHW183-PA
pHW184-HA
pHW185-NP
pHW186-NA
pHW187-M
pHW188-NS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention

Jeffrey D. Chulay, MD
Sr. VP Medical Affairs and Chief Medical Officer
AlphaVax Human Vaccines Inc.
2 Triangle Drive
Research Triangle Park, NC 27709-0307

RE: Biological Material License Agreement CDC Reference: FLU-06-052 executed June 20, 2006

Dear Dr. Chulay:

I am writing to inform you that effective June 20, 2009, the above referenced license agreement will terminate according to its terms as specified in Paragraph 6 of the Agreement. Also by the terms of the Agreement, Paragraphs 11 and 17 shall survive the Agreement's termination, as follows:

11. THE MATERIALS ARE BEING SUPPLIED WITH NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

17. LICENSEE is encouraged to publish the results of any research in scientific publications and the contribution of CDC, unless requested otherwise by CDC.

CDC does not wish to request destruction of the Materials supplied under the agreement, and hereby waives Paragraph 15, which reads:

15. Upon termination of this Agreement, LICENSEE agrees to return all Materials and Licensed Products to PHS, or provide PHS with certification of their destruction.

Moreover, CDC places no restriction on further use or further distribution of the Materials. However, if you choose to distribute Materials to others, CDC requests notification of the identity of the new recipient for tracking purposes only.

All notifications of shipment to another entity should be sent to the following address:

Centers for Disease Control and Prevention
Influenza Division, Mail Stop A20
Attn
1600 Clifton Road, NE
Atlanta, GA 30333

All correspondence relating to the Biological Material License Agreement CDC Reference: FLU-06-052 should be sent to the following address:

Centers for Disease Control and Prevention
CCID Technology Transfer, Mail Stop A42
Attn Lisa Blake DiSpigna
1600 Clifton Road, NE
Atlanta, GA 30333

Regards,

Beth P. Bell, MD MPH

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention

Acting Director,
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
1600 Clifton Road, NE
Atlanta, GA 30333

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, May 28, 2009 11:12 AM
To: Lowenhaupt, Carol (CDC/CCID/OD) (CTR)
Cc: Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Attachments: Flu Termin Ltr Flu-06-052 Alphavax (3).aw.doc

Dear Carol,

Please use the letter attached for notification to LigoCyte. You will need to edit the document to contain the appropriate information pertaining to LigoCyte. Let me review before we send anything for Beth's signature as I will want to put various emails in the signature folder.

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 5:22 PM
To: Knight, Janice (CDC/CCID/OD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Thanks. I would suggest the attached as a slightly different approach.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, May 27, 2009 4:54 PM
To: Watkins, Andrew (CDC/OD/OCSO); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

You should be able to use these.

JK

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 4:46 PM
To: Knight, Janice (CDC/CCID/OD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Is there a way to unlock the attached letter so that I may modify it? It would be much easier that way.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, May 27, 2009 3:46 PM
To: Watkins, Andrew (CDC/OD/OCSO); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Would the attached documents be appropriate?

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 3:04 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Michael et al,

There is nothing in the agreements that requires us to renew and no reason to worry about liability. The companies received what they paid for. Not renewing a license that terminates naturally would not be considered a breach of the terms of the agreement. If it is your desire to make these materials publicly available for free and with no restrictions imposed by CDC, I believe you are free to do so.

However, it might be wise to send them a formal letter waiving the requirements of Paragraph 15, which requires them to destroy or return the materials upon termination of the license. I assume that would not be your intent in opening these materials to public use.

The companies should be delighted to be able to use the materials without obligation to pay monies, so I don't see a problem If they are not delighted, I still see no problem with not renewing the license. We have not agreed to do so anywhere in the agreement.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, May 27, 2009 2:43 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Andrew,

Please find attached the executed BMLAs in question. "Natural Death" will occur mid to end of June 2009. LigoCyte is up to date on payments, Alphavax is slightly behind, but an Invoice has been issued to them.

Janice

Phone: 404 639-2679
FAX: 404 638-5465

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 2:06 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Michael,

I would like to see the agreements, but my first thought is that you can do what you want if the licenses are terminating by "natural death."

Andrew

Andrew Watkins
Director, CDC Technology Transfer Office

From: Shaw, Michael (CDC/CCID/NCIRD)
Sent: Wednesday, May 27, 2009 7:51 AM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Andrew,

We need some advice. We have been dropping all MTAs whenever possible on "live" virus but these licenses cover cDNA copies of virus genes created from HPAI isolates from Indonesia and Vietnam which, as you know, have been dealt with very carefully in the WHO/GISN negotiations on benefits and virus sharing. Both Nancy and I would prefer to drop them and let the companies deal with the countries themselves through the WHO Geneva office. This particular case is complicated by the fact that money has been received for past licensing fees. Would there be any liability for CDC if these were now dropped and the companies told they were on their own?

Janice can forward the documents if you'd like to examine them.

Michael

Michael W. Shaw, Ph.D.
Associate Director for Laboratory Science
Influenza Division, MS G-16
Centers for Disease Control and Prevention
Atlanta, GA 30333 USA

Tel.: (404)-639-1405
Fax: (404)-639-2350
Email: mws2@cdc.gov

From: Cox, Nancy (CDC/CCID/NCIRD)
Sent: Tuesday, May 26, 2009 6:44 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

We may need to seek counsel from Andrew Watkins. I would prefer to drop and let them work it out with the countries but don't know for sure if that is best way forward.
N

From: Shaw, Michael (CDC/CCID/NCIRD)
Sent: Tuesday, May 26, 2009 3:47 PM
To: Cox, Nancy (CDC/CCID/NCIRD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Nancy,

This case is not so obvious to me now that I know the details. This is for plasmid cDNA rather than the viruses themselves. Should we renew the licenses or drop them and have the companies pursue permission from Indonesia and Vietnam through WHO?

M

From: Knight, Janice (CDC/CCID/OD)
Sent: Tuesday, May 26, 2009 8:57 AM
To: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD)
Cc: Mawle, Alison (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Mike just for clarification: Early in 2006 several regular (*i.e.*, not reverse genetics related) plasmids containing Indonesian and Vietnamese genetic material were licensed to LigoCyte Pharmaceuticals and Alphavax. Both agreements expire this year in June. Shall I inform both companies that they do not need to renew the license and that they may continue to use the materials (including any derivatives) with no restrictions?

Janice

From: Shaw, Michael (CDC/CCID/NCIRD)
Sent: Saturday, May 23, 2009 12:46 PM
To: Knight, Janice (CDC/CCID/OD); Cox, Nancy (CDC/CCID/NCIRD)
Cc: Mawle, Alison (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Janice,

I concur with the proposed action. We no longer wish to exercise any control over use and further distribution of materials obtained through or derived from our role in the WHO Global Influenza Surveillance Network.

Michael

Michael W. Shaw, Ph.D.
Associate Director for Laboratory Science
Influenza Division, MS G-16
Centers for Disease Control and Prevention
Atlanta, GA 30333 USA

Tel.: (404)-639-1405
Fax: (404)-639-2350
Email: mws2@cdc.gov

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, May 22, 2009 3:31 PM
To: Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Mawle, Alison (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Dear Nancy and Mike,

In light of the recent discussions among various CDC representatives from the Influenza Division, the National Center for Immunization and Respiratory Diseases, CCID Technology Transfer, the Office of General Counsel and the NIH Branch-HHS Office of the General Counsel, it would appear that the fully executed Material Transfer Agreements CDC Reference Numbers FLU-06-045 including Amendments thereto #1 and #2 with GlaxoSmithKline and FLU-06-086 with Kaketsuken should be terminated and any request asking for an amendment to the existing agreements need not be executed (see email from GSK below). Once the MTAs are terminated GSK and Kaketsuken will not be under any restrictions on use nor distribution of the Original Materials including any modified or unmodified derivatives.

I have attached a draft Agreement to Terminate letter for your review and consideration. Your concurrence with this proposed action via email by COB May 28th will be much appreciated. GSK and Kaketsuken have been waiting a resolution to this issue for quiet some time and I would very much like to provide them with this document.

Regards,

Janice

Janice C. Knight

Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

[Out of Scope]

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Tuesday, September 01, 2009 2:21 PM
To: Berkley, Dale (NIH/OD) [E]
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Subject: RE: MTA for reverse genetics plasmids

Dale,

Thanks so much for getting back so quickly. I will check with the program to be sure that the lab doesn't plan to use the plasmid set for the purposes you outlined below. As soon as I hear from them, I will let you know the answer.

Best,

Janice

NIH

From: Knight, Janice C. (CDC)
Sent: Thursday, August 27, 2009 1:16 PM
To: Foster, Joseph A. (CDC); Berkley, Dale (NIH/OD) [E]
Cc: Blake-Dispigna, Lisa (CDC); Watkins, Andrew C. (CDC)
Subject: RE: MTA for reverse genetics plasmids

Joe, Dale,

In light of Andrew's comment, could you give me any recommendations on whether we can sign the MTA with St Jude? As I understand it the plasmid set to be provided has a different backbone to the earlier plasmids that Ruben Donis has.

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, August 27, 2009 9:48 AM
To: Foster, Joseph A. (CDC/OCOO/OD); Berkley, Dale (NIH/OD) [E]
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Knight, Janice (CDC/CCID/OD)
Subject: RE: MTA for reverse genetics plasmids

Given the previous sensitivities to this issue, I defer to OGC for their expert advice.

Andrew

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, August 26, 2009 4:59 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: FW: MTA for reverse genetics plasmids

Andrew,

The following appears in the attached proposed reverse MTA with St. Jude:

"*The Recipient acknowledges that the Materials and/or their method of production are or may be the subject of one or more patents or patent applications. Except as provided in this Agreement, no express or implied licenses or other rights are provided to the Recipient under any patents, patent applications, trade secrets or other proprietary rights of St. Jude. Recipient acknowledges no right or license is being granted by St. Jude under this MTA to commercialize or sell the Materials under any third party patents or patent applications or otherwise. To the extent any such rights or licenses are required, Recipient acknowledges that it is its responsibility to obtain such rights or licenses, as necessary. Recipient covenants that it will not use the Materials for commercial purposes such as screening, production or sale (including for any stockpile that is financially recognized by Recipient as revenue), without obtaining the necessary commercialization rights or licenses with respect thereto from (a)* (b)(4) *and its affiliates (or their respective successors), as holders of exclusive licenses of patents and/or patent applications of the reverse genetics methodology and/or products obtained using reverse genetics methods, and (b) any third parties that may have applicable rights in the Materials (or any materials used to produce Materials). Recipient acknowledges that certain restrictions set forth in this MTA are for the benefit of MedImmune, Inc. and that MedImmune, Inc. shall be deemed to be a third-party beneficiary to this MTA with the right of enforcement.*"

As you may remember we included very similar language in our earlier 2007 MTAs for distribution of influenza RG reassortants:

"*Recipient covenants that it will not use the Research Material for commercial purposes such as screening, production or sale (including for any stockpile that is financially recognized by Recipient as revenue), without obtaining the necessary commercialization rights or licenses with respect thereto from (a) MedImmune, Inc. and its affiliates (or their respective successors), as holders or exclusive licensees of patents and/or patent applications of the reverse genetics methodology and/or products obtained using reverse genetics methods, and (b) any third parties that may have applicable rights in the Research Material (or any materials used to produce the Research Material). Recipient agrees to comply with all Federal and/or National rules and regulations applicable to the Research Project and the handling of the Research Material. Recipient acknowledges that certain restrictions set forth in this MTA are for the benefit of* (b)(4) *and that* (b)(4) *shall be deemed to be a third-party beneficiary to this MTA with the right of enforcement. At the time of execution, the CDC laboratory distributing the technology and the CDC Technology Transfer Office have no knowledge of additional third party rights in the Research Material transferred by this Agreement.*" We removed this language from those MTAs as you felt we had given MedImmune enough "free advertisement" and just used the standard MTA language. Now it appears, we aren't using any legal documentation for influenza RG reassortant transfers.

So, my question: Can we sign St. Jude's MTA with as it appears above? This MTA is for RG plasmids not reassortants if that makes a difference.

Janice

From: Allay, Esther [mailto:Esther.Allay@STJUDE.ORG]
Sent: Friday, August 21, 2009 10:57 AM
To: Knight, Janice (CDC/CCID/OD)
Subject: FW: MTA for reverse genetics plasmids

Hi Janice:

I just spoke with MedImmune - they were wondering why the language in section 1 was struck. They are willing to consider this, but need an explanation before they can determine whether or not it will be acceptable. This same language is in the CDC's outgoing MTAs we have received for materials made using reverse genetics, so I'm not sure why CDC cannot agree in this MTA.

Regards,
Esther

From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
Sent: Wednesday, August 12, 2009 1:42 PM
To: Allay, Esther
Cc: Gubareva, Larisa (CDC/CCID/NCIRD)
Subject: RE: MTA for reverse genetics plasmids

Esther,

After discussions here, it is proposed the we use the version dated 12Aug09 I have attached above for this transfer. If you need to consult with MedImmune, then we will have to work within the delay.

Thanks so much,

Janice

From: Allay, Esther [mailto:Esther.Allay@STJUDE.ORG]
Sent: Tuesday, August 11, 2009 1:40 PM
To: Knight, Janice (CDC/CCID/OD)
Subject: FW: MTA for reverse genetics plasmids

Hi Janice:

Please see our comments in the attached. If you need "unmodified" in there, we will need to check with MedImmune, which may cause significant delays in executing the agreement.

Regards,
Esther

Esther R. Allay
Licensing Associate
Office of Technology Licensing - Mail Stop 742

St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Phone: 901-595-4700
FAX: 901-595-3148
email: esther.allay@stjude.org <mailto:esther.allay@stjude.org>
www.stjude.org/technology-licensing

From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
Sent: Tuesday, August 11, 2009 7:52 AM
To: Allay, Esther
Cc: Gubareva, Larisa (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA for reverse genetics plasmids

Good morning Esther,

So nice to be working with you again. I apologize for the lengthy delay in responding to Dr. Gubareva's submission of the MTA, but I do hope we can move this quickly forward. I have attached your original agreement along with a revised document for your review containing a few minor changes to the template that I hope will be acceptable based on the previous MTA we executed in 2007.

Best regards,

Janice

From: Gubareva, Larisa (CDC/CCID/NCIRD)
Sent: Tuesday, March 24, 2009 2:59 PM
To: Knight, Janice (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD); Gubareva, Larisa (CDC/CCID/NCIRD); 'Esther.Allay@stjude.org'
Subject: FW: MTA for reverse genetics plasmids
Importance: High

Hello Janice,

Could you please review the terms in the attached MTA?
Please let us know if you have any questions.

Best regards,

Larisa

From: Allay, Esther [mailto:Esther.Allay@STJUDE.ORG]
Sent: Tuesday, March 24, 2009 2:05 PM
To: Gubareva, Larisa (CDC/CCID/NCIRD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD)
Subject: MTA for reverse genetics plasmids
Importance: Low

Dear Dr. Gubareva:

Dr. Richard Webby has forwarded to me your request for the above-cited materials. St. Jude Children's Research Hospital and Dr. Webby would be pleased to provide these materials to you and the CDC under the terms of the attached Material Transfer Agreement (MTA). Whereas the terms of the MTA are designed to have minimal effect on the progress of your research, any requests to revise the terms may significantly delay completion of the MTA.

Please print out two copies of the attached MTA, sign both copies and have an authorized official of the CDC sign both. Forward both copies to me at the address below. I shall return one fully executed original to you for your files.

To expedite the transfer of materials, you may fax (901-595-3148) a copy of the signed MTA back to me provided one with original signatures follows by mail. If you have any questions, you may contact me by phone (901-595-4700) or by e-mail at: esther.allay@stjude.org.

Regards,

Esther

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FAX: 901-595-3148
email: esther.allay@stjude.org <mailto:esther.allay@stjude.org>
www.stjude.org/technology-licensing

Attachment

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, August 12, 2009 2:39 PM
To: Knight, Janice (CDC/CCID/OD)
Subject: Re: MTA for reverse genetics plasmids

In my opinion, we are free to do research with RG or RG plasmids. What a vaccine manufacturer does with it is up to them. Any issues (b)(4) may have should be with the company, not us

Not to worry.

Andrew Watkins, J.D., Ph.D.
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Sent: Wed Aug 12 14:26:54 2009
Subject: RE: MTA for reverse genetics plasmids

Yes, that is true. In your opinion, does CDC need any kind of license with MedImmune to use the RG methodology? Or so long as we don't commercialize we're ok? If Flu decides to make a flu RG reassortant for a vaccine to help in a pandemic setting and make it available to vaccine manufacturers like they do the seasonal isolates is there any problem with that so long as the manufacturer has a license with (b)(4) And what if they don't? Is this even worth worrying about?

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, August 12, 2009 2:20 PM
To: Knight, Janice (CDC/CCID/OD)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: MTA for reverse genetics plasmids

Not necessarily, but it is my understanding that those companies all have obtained licenses from med immune, so the issue is moot.

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, August 12, 2009 2:19 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: MTA for reverse genetics plasmids

PS: So far, according to Ruben Donis, the RG reassortants have been generated using CDC plasmids modified from the Oxford set sent to Yumi Matsuoka when she was here at CDC. So, if we never use any of the plasmids from MedImmune to generate the RG reassortants do we avoid obligations to them? I hope so as I think GSK, Sanofi and Novartis may have created stockpiles of vaccine for NIH using Ruben's RG reassortants>

JK

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, August 12, 2009 2:14 PM

To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: MTA for reverse genetics plasmids

Thanks so much for the quick response! Words in blue are mine that I want to insert. I thought adding unmodified was necessary and Lisa was in agreement with you to end the statement at "revenue".

Only glitch is the FLU-07-260 agreement wherein we agreed to the language and there is no termination date other than St. Jude may terminate upon 30 day notice. Does this affect the new agreement? And if this is going to be a long drawn out hassle with (b)(4) as per Esther Allay, is changing the document worth it since we agreed to it before?

JK

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, August 12, 2009 2:03 PM
To: Knight, Janice (CDC/CCID/OD); Foster, Joseph A. (CDC/OCOO/OD)
Subject: RE: MTA for reverse genetics plasmids

Janice,

Are the words in blue words that you want to add, or they words you want to delete? I think "unmodified" derivatives should be correct as it appears in the original MTA with Rubin.

As to (b)(4) issue, I would offer to end the sentence at "revenue)." That way, if we simply promise not to ever commercialize their material, then we shouldn't need to worry about needing a license or permission from (b)(4) or any one else.

To me, article 2 i) is fine if that is a promise that we plan to actually live up to.

Andrew

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, August 12, 2009 1:36 PM
To: Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Subject: FW: MTA for reverse genetics plasmids
Importance: High

Andrew, Joe,

It has been about 2 years since we executed a reverse agreement (see pdf Flu-07-260) with St Jude for their reverse genetics plasmid set and I just want to be sure that the terms of the attached agreement are still acceptable. Particularly the following:

Article 1.

i) First sentence: definition of materials to include derivatives as opposed to "unmodified" derivatives which is unacceptable to us.

ii) Seventh sentence: Recipient covenants that it will not use the Materials for commercial purposes such as screening, production or sale (including for any stockpile that is financially recognized by Recipient as revenue), without obtaining the necessary commercialization rights or licenses with respect thereto from (a) MedImmune, Inc. and its affiliates (or their respective successors), as holders of exclusive licenses of patents and/or patent applications of the reverse genetics methodology and/or products obtained using reverse genetics methods, and (b) any third parties that may have applicable rights in the Materials (or any materials used to produce Materials). Recipient acknowledges that certain restrictions set forth in this MTA are for the benefit of (b)(4) and that MedImmune, Inc. shall be deemed to be a third-party beneficiary to this MTA with the right of enforcement.

Article 2.

i) The Materials will be used exclusively for non-clinical, non-commercial research by Recipient, and will not under any circumstances be used in humans or in any process used to make a product intended for use in humans.

Thanks,

Janice

From: Allay, Esther [mailto:Esther.Allay@STJUDE.ORG]
Sent: Tuesday, August 11, 2009 1:40 PM
To: Knight, Janice (CDC/CCID/OD)
Subject: FW: MTA for reverse genetics plasmids

Hi Janice:

Please see our comments in the attached. If you need "unmodified" in there, we will need to check with (b)(4) which may cause significant delays in executing the agreement.

Regards,
Esther

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www.stjude.org/technology-licensing

From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
Sent: Tuesday, August 11, 2009 7:52 AM
To: Allay, Esther
Cc: Gubareva, Larisa (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA for reverse genetics plasmids

Good morning Esther,

So nice to be working with you again. I apologize for the lengthy delay in responding to Dr. Gubareva's submission of the MTA, but I do hope we can move this quickly forward. I have attached your original agreement along with a revised document for your review containing a few minor changes to the template that I hope will be acceptable based on the previous MTA we executed in 2007.

Best regards,

Janice

From: Gubareva, Larisa (CDC/CCID/NCIRD)
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To: Knight, Janice (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD); Gubareva, Larisa (CDC/CCID/NCIRD); 'Esther.Allay@stjude.org'
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Hello Janice,

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Larisa

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Sent: Tuesday, March 24, 2009 2:05 PM
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From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
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To: Allay, Esther
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Subject: RE: MTA for reverse genetics plasmids

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To: Knight, Janice (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD); Gubareva, Larisa (CDC/CCID/NCIRD); 'Esther.Allay@stjude.org'
Subject: FW: MTA for reverse genetics plasmids
Importance: High

Hello Janice,

Could you please review the terms in the attached MTA?

Please let us know if you have any questions.

Best regards,

Larisa

From: Allay, Esther [mailto:Esther.Allay@STJUDE.ORG]
Sent: Tuesday, March 24, 2009 2:05 PM
To: Gubareva, Larisa (CDC/CCID/NCIRD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD)
Subject: MTA for reverse genetics plasmids
Importance: Low

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Regards,

Esther

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www.stjude.org/technology-licensing

Attachment

Email Disclaimer: www.stjude.org/emaildisclaimer

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, June 18, 2009 12:42 PM
To: Watkins, Andrew (CDC/OD/OCSO); Welch, Alice Y. (FDA)
Cc: Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: QUESTION re MTAs that CDC uses for pandemic flu strain sharing
Attachments: Biosafety Recommendations for swH1N1 Virus shipment insert.doc; swH1N1 Virus shipment insert (rev).doc

I have attached the most current version of the package insert that accompanies the H1N1 viruses.

Janice

From: Knight, Janice (CDC/CCID/OD)
Sent: Tuesday, June 16, 2009 10:14 AM
To: Watkins, Andrew (CDC/OD/OCSO); Welch, Alice Y. (FDA)
Subject: RE: QUESTION re MTAs that CDC uses for pandemic flu strain sharing

I will need to contact Dr. Ruben Donis for the most current version of the language included as the package insert. I hope to hear from him today and will forward as soon as I receive the documents.

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Tuesday, June 16, 2009 8:13 AM
To: Knight, Janice (CDC/CCID/OD); Welch, Alice Y. (FDA)
Subject: RE: QUESTION re MTAs that CDC uses for pandemic flu strain sharing

Thanks Janice. Would you mind sharing the current label language with FDA?

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Tuesday, June 16, 2009 7:46 AM
To: Watkins, Andrew (CDC/OD/OCSO); Welch, Alice Y. (FDA)
Subject: RE: QUESTION re MTAs that CDC uses for pandemic flu strain sharing

Yes, Andrew, your statement is in line with current internal Influenza Division policies.

Regards,

Janice
Janice Knight
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention

CCID Technology Transfer
Phone: 404 639-2679
FAX: 404 638-5465

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Monday, June 15, 2009 1:25 PM
To: Welch, Alice Y. (FDA); Knight, Janice (CDC/CCID/OD)
Subject: RE: QUESTION re MTAs that CDC uses for pandemic flu strain sharing

Hi Alice,

We no longer use an MTA that specifically references (b)(4) All the major manufacturers have now taken licenses from (b)(4) In fact, we no longer use an MTA to distribute any live attenuated influenza vaccine virus. We are now providing them with a pretty simple label only, that disclaims warranty/indemnity and suggests that the recipient be responsible for doing their own freedom to operate due diligence. And we request that they inform us of to whom further distribute the virus.

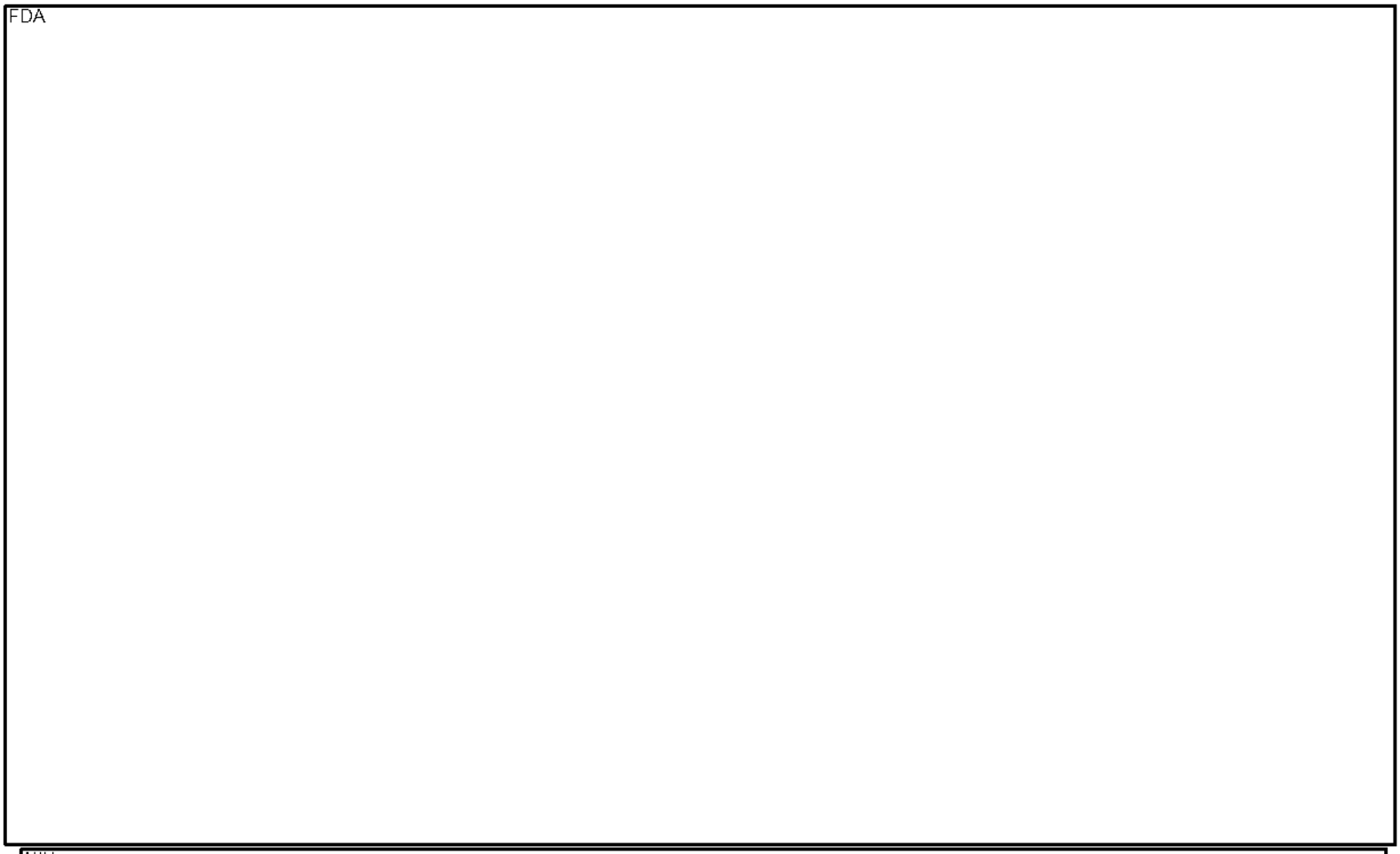
Janice, can you confirm that this would cover the virus that Alice is planning to share, and the actual label language?

Of course, Alice, this is as yet an internal CDC policy on flu vaccine virus distribution, but it was developed in coordination and with the support (prodding?) of HHS OGC (Dale).

Thanks, Andrew

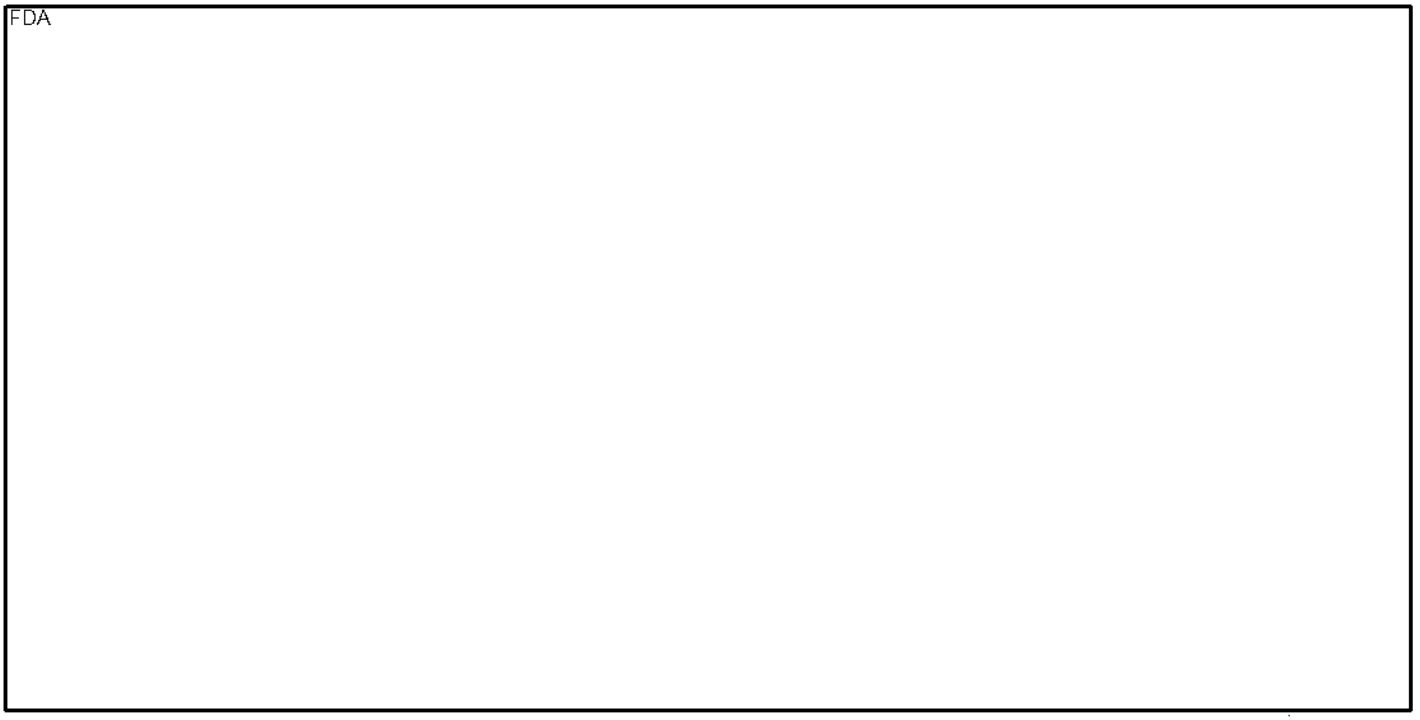
Andrew Watkins
Director, CDC Technology Transfer Office

FDA


FDA


NIH


FDA


FDA

Biosafety recommendations for *in vitro* laboratory work with novel swine-origin H1N1 influenza virus:

General laboratory work, including growth of virus in cell culture or embryonated eggs should be performed in a BSL2 laboratory with BSL3 practices. All viral manipulations should be done inside a BSC that is certified annually.

Personal protective equipment may include the following based on a site specific risk assessment:

- Respiratory protection – fit-tested N95 respirator or higher level of protection.
- Shoe covers
- Closed-front gown
- Double gloves
- Eye protection

Laboratory waste

All waste disposal procedures should be followed as outlined in your facility standard laboratory operating procedures. Steam autoclaving is the preferred method for all decontamination processes. Alternative methods may be considered based on a site specific risk assessment.

Appropriate disinfectants

Several chemical disinfectants, including chlorine, alcohols, peroxygen, detergents, iodophors, quaternary ammonium and phenolic compounds, are effective against human influenza viruses if used at the correct concentration for the appropriate contact time as specified in the manufacturer's recommendations.

Occupational Health

All personnel should self monitor for fever and other symptoms such as cough, sore throat, runny or stuffy nose, body aches, headache, chills, and fatigue. Any influenza-like illness should be reported to your supervisor immediately.

Personnel who have had an occupational exposure to clinical material or live virus from a confirmed case of novel influenza A (H1N1) should immediately report to their supervisor. Antiviral chemoprophylaxis should be considered, For additional information on antiviral treatment visit: Interim Guidance on Antiviral Recommendations for Patients with Confirmed or Suspected Swine Influenza A (H1N1) Virus Infection and Close Contacts

For additional information: Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition

THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS. This Research Material, provided at the discretion of CDC, will be used by Recipient under suitable containment conditions. Recipient agrees to comply with all Federal rules and regulations applicable to the Research Project and the handling of the Research Material. Current CDC recommendations for the handling of novel swine-origin H1N1 influenza viruses can be found at http://www.cdc.gov/h1n1flu/guidelines_labworkers.htm which are summarized in the attached sheet.

THE MATERIALS ARE BEING SUPPLIED WITH NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

AT THE REQUEST OF USDA, CDC STRONGLY RECOMMENDS THAT THE ENCLOSED VIRUS SAMPLES ARE:

1) not used for *in vivo* studies involving swine, poultry and other livestock species without contacting USDA/APHIS/VS at 301-734-7783 or 301-734-3277 to ascertain the biosafety precautions that must be used in order to protect US swine, poultry and other livestock species population from inadvertent infection;

and,

2) only further distributed to other laboratories for public health and research purposes and not for *in vivo* studies involving swine, poultry and other livestock species.

In all oral presentations and written publications concerning this Material, you will acknowledge our contribution in a mutually acceptable manner.

Unless Recipient is an academic or non-profit entity, Recipient agrees to hold the United States Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses, and losses arising out of Recipient's use for any purpose of the Research Material.

Recipient understands that the supplied material may pose health risks to laboratory workers, the community, and the environment. Recipient agrees to employ the appropriate biosafety standards including special practices, equipment and facilities as necessary, and will comply with all applicable Recipient and Government health and safety regulations.

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Monday, June 15, 2009 1:25 PM
To: Welch, Alice Y. (FDA); Knight, Janice (CDC/CCID/OD)
Subject: RE: QUESTION re MTAs that CDC uses for pandemic flu strain sharing

Hi Alice,

We no longer use an MTA that specifically references Medimmune. All the major manufacturers have now taken licenses from (b)(4) n fact, we no longer use an MTA to distribute any live attenuated influenza vaccine virus. We are now providing them with a pretty simple label only, that disclaims warranty/indemnity and suggests that the recipient be responsible for doing their own freedom to operate due diligence. And we request that they inform us of to whom further distribute the virus.

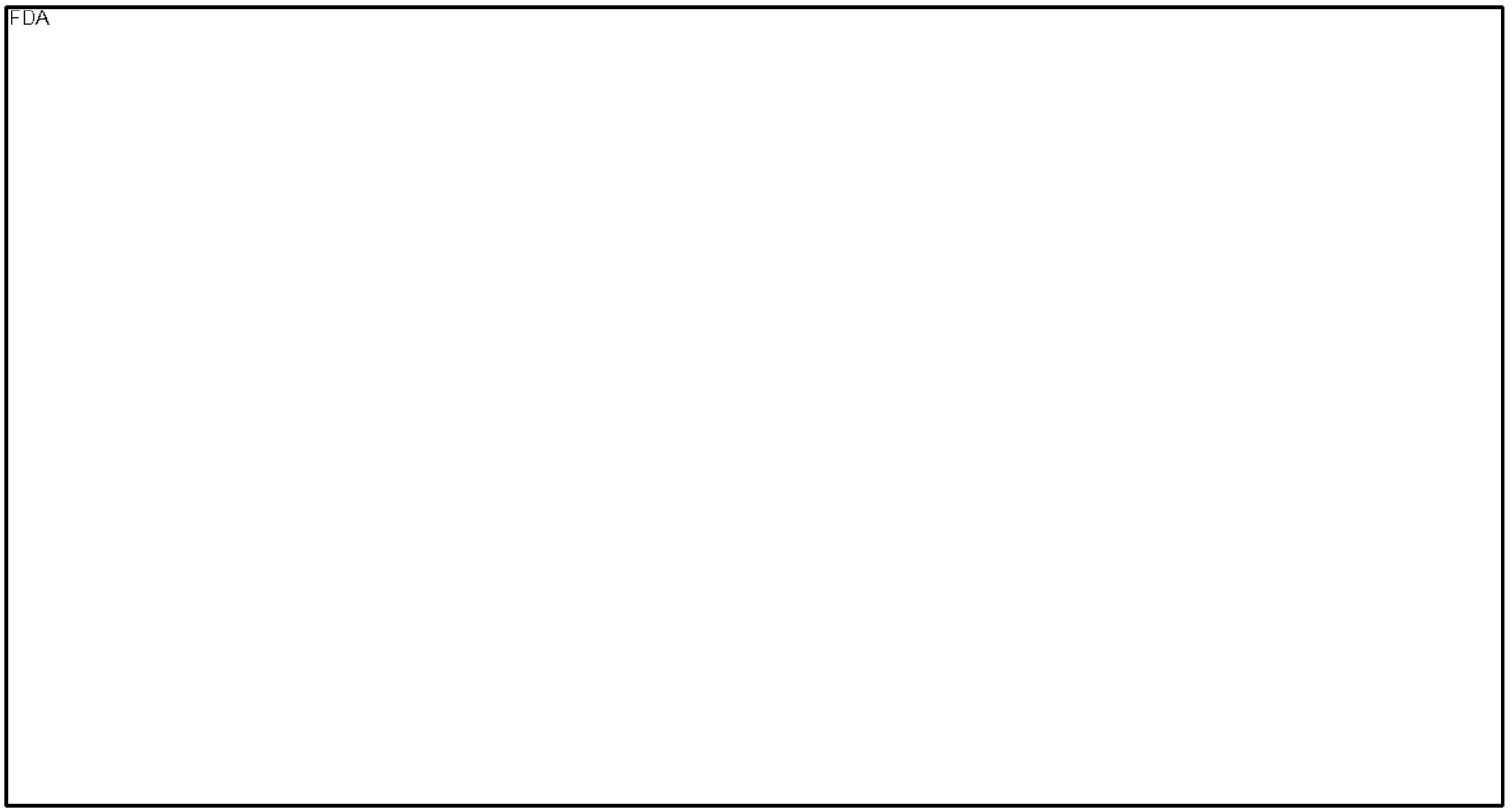
Janice, can you confirm that this would cover the virus that Alice is planning to share, and the actual label language?

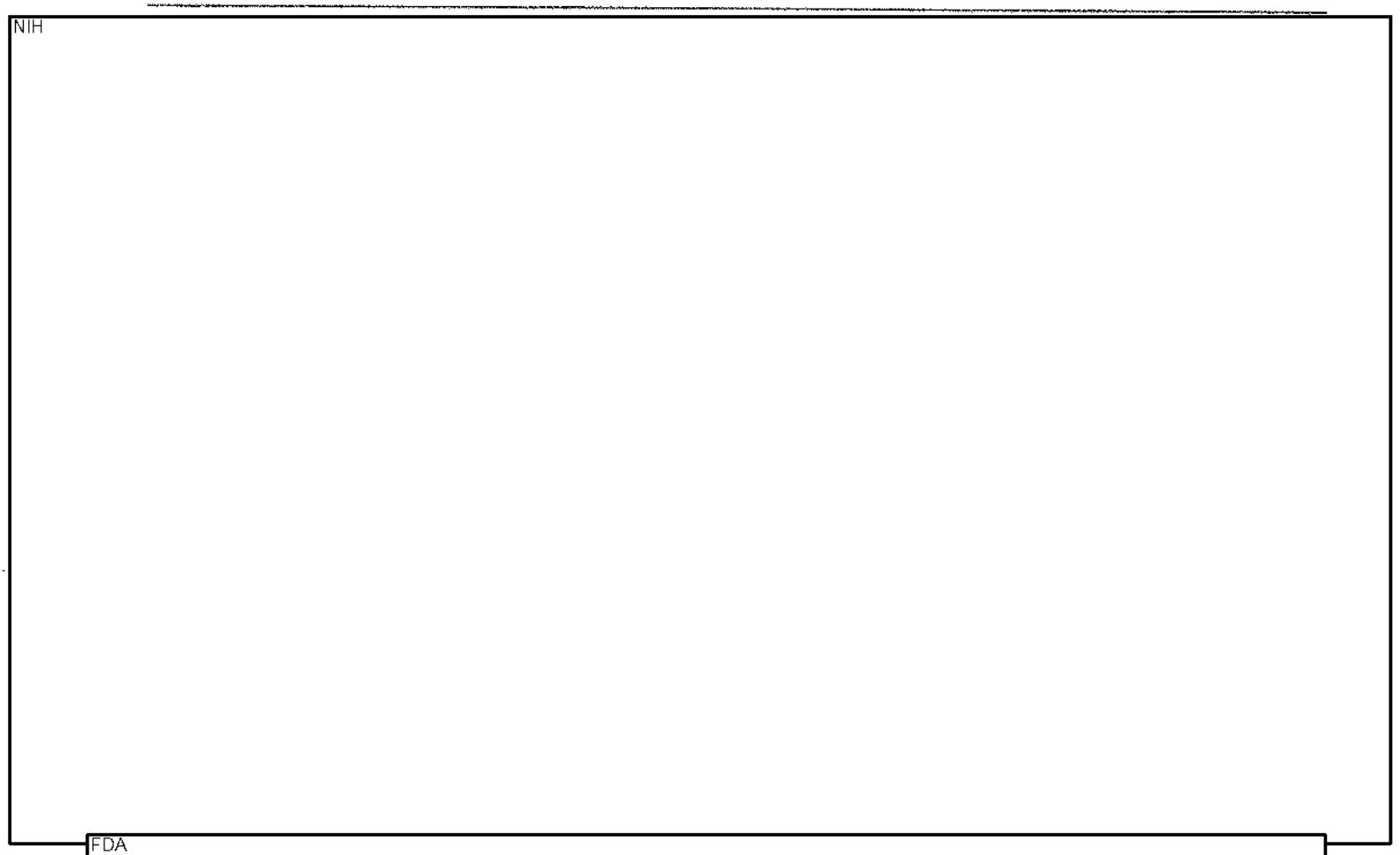
Of course, Alice, this is as yet an internal CDC policy on flu vaccine virus distribution, but it was developed in coordination and with the support (prodding?) of HHS OGC (Dale).

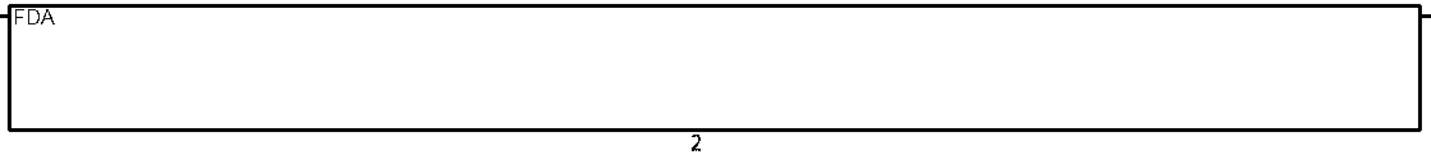
Thanks, Andrew

Andrew Watkins
Director, CDC Technology Transfer Office

FDA


FDA


NIH


FDA

FDA

FDA

Hiroshi Mizokami, PhD
Executive Managing Director
Board of Directors
Kaketsuken, Japan
Kikuchi Research Center Kyokushi

RE: Material Transfer Agreement CDC Reference: FLU-06-086 executed September 26, 2006

Dear Dr. Mizokami,

I am writing to inform you as the Executive Managing Director, Board of Directors, Kaketsuken that effective June 01, 2009, the Centers for Disease Control and Prevention wishes to terminate the above referenced transfer Agreement. Referencing the terms of the original Agreement, Paragraphs 6 and 11 shall survive the Agreement's termination, as follows:

6. THE MATERIALS ARE BEING SUPPLIED WITH NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE and with no guarantee that the use of the Material will not infringe any patent or proprietary rights of third parties.

11a. The supplied Materials may pose health risks to laboratory workers, the community, and the environment. CDC recommends that the Recipient employ the appropriate biosafety standards including special practices, equipment and facilities as necessary, and recommends compliance with all applicable Recipient and Government health and safety regulations as described in the Appendix A. Note: If Recipient is not governed by US Law, Recipient is advised to follow all rules and regulations stipulated by the country in which Recipient resides or by International Agencies such as the World Health Organization.

11b. Recipient is encouraged to publish the results of any research in scientific publications and the contribution of CDC, unless requested otherwise by CDC.

CDC does not wish to request destruction of the Materials supplied under the agreement, and hereby waives Paragraph 5, which reads:

5. This Research Material represents a significant investment on the part of Provider, and is considered proprietary to Provider. Recipient's investigator therefore agrees to retain control over this Research Material, and further agrees not to transfer the Research Material to others not under his or her direct supervision without advance written approval of Provider. Provider reserves the right to distribute the Research Material to others and to use it for its own purposes. When the Research Project is completed, or three (3) years have elapsed from receipt of Research Material, whichever occurs first, the Research Material will be destroyed by Recipient or otherwise disposed of as mutually agreed by Provider and Recipient.

Moreover, CDC places no restriction on further use or further distribution of the Materials. However, if you choose to distribute Materials to others, CDC requests notification of the identity of the new recipient for tracking purposes only.

All notifications of shipment to another entity should be sent to the following address:

Centers for Disease Control and Prevention
Influenza Division, Mail Stop A20
Attn Mary Hoelscher
1600 Clifton Road, NE
Atlanta, GA 30333

All correspondence relating to the Material Transfer Agreement CDC Reference: FLU-06-086 should be sent to the following address:

Centers for Disease Control and Prevention
CCID Technology Transfer, Mail Stop A42
Attn Lisa Blake DiSpigna
1600 Clifton Road, NE
Atlanta, GA 30333

Regards,

Beth P. Bell, MD MPH
Acting Director, National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
1600 Clifton Road, NE
Atlanta, GA 30333

Enclosure: Appendix A

APPENDIX A

Influenza Branch/DVRD/NCID Biosafety recommendations for laboratory handling of high growth PR8 reassortants of influenza virus bearing engineered H5 HA derived from highly pathogenic avian influenza virus strains.

Definitions: This appendix concerns the use of vaccine reference stocks of reassortant viruses carrying the internal genes from A/PR/8/34, and the surface genes from highly pathogenic avian influenza (HPAI) strains (e.g., H5N1). The reassortant virus is considered to be equivalent to the H5 low pathogenicity avian influenza (LPAI) viruses with regards to its virulence properties. These reassortants are referred to as DeltaH5-PR8 candidate vaccine reference stocks. Information on risk assessment of these reference vaccine stocks can be obtained at the WHO website URL: www.who.int/entity/csr/resources/publications/influenza/en/influenzaRMD2003_5.pdf.

Risk assessment: The A/PR/8/34 is considered to be attenuated in humans. The A/PR/8/34 has virulence properties equivalent to LPAI strains. There are no documented human infections with strains of the H5 subtype of LPAI. Therefore, the reassortants are predicted to pose a minimal risk to humans. However, caution is necessary because of the limited experience with vaccine strains possessing a combination of avian genes and genes from a human virus, albeit egg-adapted. While the DeltaH5-PR8 virus is expected to be replication-deficient in humans, there is a remote possibility of secondary reassortment with a normal human influenza A virus which could generate a replication-competent virus.

Laboratory hazards: The primary laboratory hazard is inhalation of DeltaH5-PR8 virus or mucosal exposure from aerosols generated by aspirating, dispensing, mixing, centrifuging or otherwise manipulating virus-infected samples.

Recommended Precautions: Biosafety Level 2 facilities, with enhanced practices and procedures are recommended for research and production activities utilizing live DeltaH5-PR8 candidate vaccine reference stocks.

The enhancements beyond all the applicable BSL2 protocols include:

1) The laboratory where work with DeltaH5-PR8 is performed should have negative pressure relative to the atmosphere and adjacent hallways or laboratories with direct access.

2) All manipulations of open containers with DeltaH5-PR8 candidate vaccine reference stocks should be performed in a class II biological safety cabinet. However this may not be possible in a manufacturing environment and alternative control measures are therefore needed:
   a. use of other suitable barrier systems;
   b. staff should use of powered full-face respirators, equipped with HEPA filters;
   c. antiviral prophylaxis for staff in the production area and those in adjacent areas. Neuraminidase inhibitor antiviral drugs (e.g., oseltamivir, zanamivir) should be available for treatment and post-exposure prophylaxis, as necessary (MMWR May 28, 2004 / 53(RR06);1-40).

3) There should be no need to inactivate effluent from sinks, because any liquid effluent from sinks should have been disinfected by validated procedures and there is little risk of hand-washing effluent posing a hazard to the environment.

4) A code of practice for the work should be prepared, the key features of which are:

   a. Access to the laboratory is restricted to authorized personnel. A sign should be posted at the entrance door during the times that experiments are in progress to indicate this fact. No other experiment of any kind should be conducted simultaneously in the same room where the DeltaH5-PR8 reassortant is being used.
   b. Personnel should wear complete protective gear, including head cover, goggles, N95 nose and face mask, gown, and booties. Double gloves should be used to allow safe disposal of all the protective gear into an autoclave bag within the room.

c. Showering is not required, as protective clothing and hand washing procedures are normally considered adequate to protect human health and the environment for this level of hazard.
d. Procedures to prevent exposure of the H5N1 reassortant to normal human and animal influenza viruses. Staff should have received a conventional influenza vaccine to limit their susceptibility to infection with normal human viruses. If pilot lots of DeltaH5-PR8 vaccine are available, staff should receive them.
e. There should also be an Occupational Health Policy for antiviral prophylaxis or for treatment following accidental exposure to the DeltaH5-PR8 reassortant virus. All personnel at risk should be enrolled in an appropriately constituted respiratory protection program. Personnel should be counseled regarding the risks and monitored for disease symptoms and absenteeism. Personnel should monitor their body temperature daily and report any fever (temperature >38 °C or 100.4 °F) if accompanied by sore throat and cough and/or dyspnea (difficult respiration or laborious breathing).
f. Review of all working practices to minimize the creation of aerosols from the vaccine virus.
g. Standard Operating Procedures for the safe decontamination of waste and equipment should be established.
h. Emergency procedures for events such as spillages documented.
i. The staff biosafety training program should document the proficiency of the trainees.

5) All virus samples that are not saved for future use in a secure location should be autoclaved immediately and discarded.

6) Storage of baseline serum samples from individuals working with these influenza strains is recommended.

PUBLIC HEALTH SERVICE MATERIAL TRANSFER AGREEMENT

This Material Transfer Agreement ("MTA") has been adopted for use by the National Institutes of Health, the Food and Drug Administration and the Centers for Disease Control and Prevention, collectively referred to herein as the Public Health Service ("PHS") in all transfers of research material (Research Material) whether PHS is identified below as its Provider or Recipient.

Provider: **Centers for Disease Control and Prevetion**

Recipient: **Kaketsuken**

Provider authorizes the National Institute of Infectious Diseases, Tokyo, Japan (CDC Ref: Flu-06-074) to transfer to Recipient's investigator named below the following **Original Material:**

Influenza A virus reassortant Indo/05/2005(H5N1)/PR8-IBCDC-RG2 reference strain.

Research Material includes Original Material, Progeny, and Unmodified Derivatives. The Research Material shall not include: (a) Modifications, or (b) other substances created by the Recipient through the use of the Research Material which are not Modifications, Progeny, or Unmodified Derivatives.
Progeny: Unmodified descendant from the Research Material such as virus from virus, cell from cell, or organism from organism.
Unmodified Derivatives: Substances created by the Recipient which constitute an unmodified functional subunit or product expressed by the Original Material or containing changes (e.g., mutations) that arise during the process of passaging through or adapting to a substrate (e.g., a cell line or eggs). Some examples include: adaptive mutants of virus strains, subclones of unmodified cell lines, purified or fractionated subsets of the Original Material, proteins expressed by DNA/RNA supplied by the Provider, or monoclonal antibodies secreted by a hybridoma cell line.
Modifications: Substances created by the Recipient which contain/incorporate the Research Material.

1. **Research Material will only be used for research purposes by Recipient for the Research Project described below, under suitable containment conditions. Notwithstanding anything to the contrary in the description of the Research Project or elsewhere in this MTA, Recipient acknowledges no right or license is being granted by Provider under this MTA to commercialize or sell the Research Material under any third party patents or patent applications or otherwise. To the extent any such rights or licenses are required, Recipient acknowledges that it is its responsibility to obtain such rights or licenses, as necessary. Recipient covenants that it will not use the Research Material for commercial purposes such as screening, production or sale (including for any stockpile that is financially recognized by Recipient as revenue), without obtaining the necessary commercialization rights or licenses with respect thereto from (a) (b)(4) and its affiliates (or their respective successors), as holders or exclusive licensees of patents and/or patent applications of the reverse genetics methodology and/or products obtained using reverse genetics methods, and (b) any third parties that may have applicable rights in the Research Material (or any materials used to produce the Research Material). Recipient agrees to comply with all Federal and/or National rules and regulations applicable to the Research Project and the handling of the Research Material. Recipient acknowledges that certain restrictions set forth in this MTA are for the benefit of (b)(4) and that (b)(4) shall be deemed to be a third-party beneficiary to this MTA with the right of enforcement. At the time of execution, the CDC laboratory distributing the**

knowledge of additional third party rights in the Research Material transferred by this Agreement.

2. Are the Research Materials of human origin?

☐ Yes

☒ No

If Yes, were Research Materials collected according to 45 CFR Part 46, "Protection of Human Subjects"?

☐ Yes (Please provide Assurance Number: ____)
☐ No

3. **This Research Material will be used by Recipient's investigator <u>solely</u> in connection with the following research project; please check each box that applies:**

a. ☑ Generation of virus seed for production of pilot lots of inactivated candidate vaccines for use in human clinical trials.
b. ☐ Generation of virus seed for production of pilot lots of inactivated vaccines for use in animals.
c. ☑ For in vitro studies to assess immune responses to H5N1 in humans or animals.
d. ☑ For in vivo studies in laboratory animals to assess immune responses to H5N1.
e. ☐ Other - **Please attach a brief description of research project to the agreement.**

4. In all oral presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's contribution of this Research Material unless requested otherwise. To the extent permitted by law, Recipient agrees to treat in confidence, for a period of three (3) years from the date of its disclosure, any of Provider's written information about this Research Material that is stamped "CONFIDENTIAL," except for information that was previously known to Recipient or that is or becomes publicly available or which is disclosed to Recipient without a confidentiality obligation or that the Recipient can establish by reasonable proof is independently developed by employees of the Recipient who had no knowledge of the confidential information disclosed. Any oral disclosures from Provider to Recipient shall be identified as being CONFIDENTIAL by notice delivered to Recipient within ten (10) days after the date of the oral disclosure. Recipient may publish or otherwise publicly disclose the results of the Research Project, but if Provider has given CONFIDENTIAL information to Recipient such public disclosure may be made only after Provider has had thirty (30) days to review the proposed disclosure to determine if it includes any CONFIDENTIAL information, except when a shortened time period under court order or the Freedom of Information Act pertains.

5. This Research Material represents a significant investment on the part of Provider, and is considered proprietary to Provider. Recipient's investigator therefore agrees to retain control over this Research Material, and further agrees not to transfer the Research Material to others not under his or her direct supervision without advance written approval of Provider. Provider reserves the right to distribute the Research Material to others and to use it for its own purposes. When the Research Project is completed, or three (3) years have elapsed from receipt of Research Material, whichever occurs first, the Research Material will

be destroyed by Recipient or otherwise disposed of as mutually agreed by Provider and Recipient.

6. This Research Material is provided as a service to the research community. IT IS BEING SUPPLIED TO RECIPIENT WITH NO WARRANTIES, EXPRESSED OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Provider makes no representations that the use of the Research Material will not infringe any patent or proprietary rights of third parties.

7. When Provider is PHS: Recipient shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the Research Project. Recipient agrees not to claim, infer, or imply Governmental endorsement of the Research Project, the institution or personnel conducting the Research Project or any resulting commercial product(s). Recipient agrees to hold the United States Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses, and losses arising out of Recipient's use for any purpose of the Research Material.

8. When the recipient is PHS: The PHS shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the Research Project. The PHS is not authorized to promise rights in advance for inventions developed under this Agreement. Provider acquires no intellectual property rights under this MTA, but may apply for license rights to any patentable invention that might result from this Research Project. It is the intention of CDC that Provider not be liable to PHS for any claims or damages arising from PHS's use of the Research Material; however, no indemnification is provided or intended.

9. The undersigned Provider and Recipient expressly certify and affirm that the contents of any statements made herein are truthful and accurate.

10. This MTA shall be construed in accordance with Federal law as applied by the Federal courts in the District of Columbia.

11. Any additional requirements:

    a. **Recipient's Biosafety Official shall accept full responsibility for the safety of the Research Project and that the Research Project will be performed in accordance with applicable institution and Government health and safety regulations and the guidelines detailed in Appendix A[1], as well as *Biosafety in Microbiological and Biomedical Laboratories*, 4th Edition, GPO Stock No. 017-040-00547-4, May 1999, or the most recent revision of these guidelines.**
    b. **No later than one month before a publication concerning the results obtained with the Research Material is going to be submitted, Recipient agrees to send a copy or draft of the paper to the Provider's Investigator. If there is no publication, the Recipient agrees to communicate the results of the studies concerning the Research Material to the Provider's Investigator. Any such results shall be kept in confidence in accordance with the Freedom of Information Act (5 U.S.C. ' 552), Department of Health and Human Services regulations (45 C.F.R. ' 5.65), and Executive Order No. 12600.**
    c. **In all publications related to the Research Material, its origin and the name given by the Provider must be indicated.**

[1]Appendix A. The Influenza Branch guidelines for the recommended BSL2-enhanced safety procedures for the handling of the Research Material.

NEXT PAGE SIGNATURE PAGE

PUBLIC HEALTH SERVICE MATERIAL TRANSFER AGREEMENT

Certification of Recipient Scientist: **I have read and understood the conditions outlined in this Agreement, and I understand that I must abide by them to receive and use the Research Material.**

RECIPIENT INVESTIGATOR:

Signature: Shuro Goto Date: September 2, 2006

Name: Shuro Goto
Title: Deputy General Manager, First Production Department

RECIPIENT'S BIOSAFETY OFFICIAL:

Signature: Sachio Tokiyoshi Date: September 2, 2006
Name of Biosafety Official: Sachio Tokiyoshi, D.V.M., Ph.D.
Telephone number: (81)968-37-4055

AUTHORIZED OFFICIAL FOR RECIPIENT:

Signature: A. Tashiro Date: September 2, 2006

Name: Akira Tashiro, Ph.D.
Title: Executive Managing Director, Board of Directors

Recipient's Mailing Address:

Kaketsuken,
1-6-1 Okubo, Kumamoto-shi, Kumamoto, 860-8568, Japan

PROVIDER INVESTIGATOR: Ruben Donis, Ph.D.
Chief, Molecular Genetics Section, Influenza Branch

AUTHORIZED OFFICIAL FOR PROVIDER:

Signature: Kenneth L Kellen Date: 9/26/2006

for Rima Khabbaz, M.D.
Director, National Center for Infectious Diseases

Provider's Mailing Address: Centers for Disease Control and Prevention
1600 Clifton Road, N.E.,
(Mail Stop A-42 Attn. NCID Technology Coordinator Office)
Atlanta, Georgia 30333

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, June 03, 2009 2:08 PM
To: Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO); Berkley, Dale (NIH/OD) [E]
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Attachments: Flu Termin Ltr FLU-06-086 Kaketsuken-09.doc; FLU-06-086 Kaketsuken.pdf

Importance: High

I have modeled a termination letter for the MTAs governing the transfer of the reverse genetics influenza reassortants in accordance with the recommendations from CDC Influenza Division on a document provided by Andrew for termination of a BMLA. Before I use the MTA termination letter, I ask that you review and send me your comments. I have attached the MTA in question along with my draft letter of termination for Kaketsuken, FLU-06-086.

Your kind and prompt attention to this will be very, very appreciated.

Janice

Janice C. Knight
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 5:22 PM
To: Knight, Janice (CDC/CCID/OD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Thanks. I would suggest the attached as a slightly different approach.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, May 27, 2009 4:54 PM
To: Watkins, Andrew (CDC/OD/OCSO); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

You should be able to use these.

JK

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 4:46 PM
To: Knight, Janice (CDC/CCID/OD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Is there a way to unlock the attached letter so that I may modify it? It would be much easier that way.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, May 27, 2009 3:46 PM
To: Watkins, Andrew (CDC/OD/OCSO); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Would the attached documents be appropriate?

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 3:04 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Michael et al,

There is nothing in the agreements that requires us to renew and no reason to worry about liability. The companies received what they paid for. Not renewing a license that terminates naturally would not be considered a breach of the terms of the agreement. If it is your desire to make these materials publicly available for free and with no restrictions imposed by CDC, I believe you are free to do so.

However, it might be wise to send them a formal letter waiving the requirements of Paragraph 15, which requires them to destroy or return the materials upon termination of the license. I assume that would not be your intent in opening these materials to public use.

The companies should be delighted to be able to use the materials without obligation to pay monies, so I don't see a problem. If they are not delighted, I still see no problem with not renewing the license. We have not agreed to do so anywhere in the agreement.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, May 27, 2009 2:43 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Andrew,

Please find attached the executed BMLAs in question. "Natural Death" will occur mid to end of June 2009. LigoCyte is up to date on payments, Alphavax is slightly behind, but an Invoice has been issued to them.

Janice

Phone: 404 639-2679
FAX: 404 638-5465

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 2:06 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Michael,

I would like to see the agreements, but my first thought is that you can do what you want if the licenses are terminating by "natural death."

Andrew

Andrew Watkins
Director, CDC Technology Transfer Office

From: Shaw, Michael (CDC/CCID/NCIRD)
Sent: Wednesday, May 27, 2009 7:51 AM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)

Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Andrew,

We need some advice. We have been dropping all MTAs whenever possible on "live" virus but these licenses cover cDNA copies of virus genes created from HPAI isolates from Indonesia and Vietnam which, as you know, have been dealt with very carefully in the WHO/GISN negotiations on benefits and virus sharing. Both Nancy and I would prefer to drop them and let the companies deal with the countries themselves through the WHO Geneva office. This particular case is complicated by the fact that money has been received for past licensing fees. Would there be any liability for CDC if these were now dropped and the companies told they were on their own?

Janice can forward the documents if you'd like to examine them.

Michael

Michael W. Shaw, Ph.D.
Associate Director for Laboratory Science
Influenza Division, MS G-16
Centers for Disease Control and Prevention
Atlanta, GA 30333 USA

Tel.: (404)-639-1405
Fax: (404)-639-2350
Email: mws2@cdc.gov

From: Cox, Nancy (CDC/CCID/NCIRD)
Sent: Tuesday, May 26, 2009 6:44 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

We may need to seek counsel from Andrew Watkins. I would prefer to drop and let them work it out with the countries but don't know for sure if that is best way forward.
N

From: Shaw, Michael (CDC/CCID/NCIRD)
Sent: Tuesday, May 26, 2009 3:47 PM
To: Cox, Nancy (CDC/CCID/NCIRD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Nancy,

This case is not so obvious to me now that I know the details. This is for plasmid cDNA rather than the viruses themselves. Should we renew the licenses or drop them and have the companies pursue permission from Indonesia and Vietnam through WHO?

M

From: Knight, Janice (CDC/CCID/OD)
Sent: Tuesday, May 26, 2009 8:57 AM
To: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD)
Cc: Mawle, Alison (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)

Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Mike just for clarification: Early in 2006 several regular (*i.e.*, not reverse genetics related) plasmids containing Indonesian and Vietnamese genetic material were licensed to LigoCyte Pharmaceuticals and Alphavax. Both agreements expire this year in June. Shall I inform both companies that they do not need to renew the license and that they may continue to use the materials (including any derivatives) with no restrictions?

Janice

From: Shaw, Michael (CDC/CCID/NCIRD)
Sent: Saturday, May 23, 2009 12:46 PM
To: Knight, Janice (CDC/CCID/OD); Cox, Nancy (CDC/CCID/NCIRD)
Cc: Mawle, Alison (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Janice,

I concur with the proposed action. We no longer wish to exercise any control over use and further distribution of materials obtained through or derived from our role in the WHO Global Influenza Surveillance Network.

Michael

Michael W. Shaw, Ph.D.
Associate Director for Laboratory Science
Influenza Division, MS G-16
Centers for Disease Control and Prevention
Atlanta, GA 30333 USA

Tel.: (404)-639-1405
Fax: (404)-639-2350
Email: mws2@cdc.gov

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, May 22, 2009 3:31 PM
To: Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Mawle, Alison (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Dear Nancy and Mike,

In light of the recent discussions among various CDC representatives from the Influenza Division, the National Center for Immunization and Respiratory Diseases, CCID Technology Transfer, the Office of General Counsel and the NIH Branch-HHS Office of the General Counsel, it would appear that the fully executed Material Transfer Agreements CDC Reference Numbers FLU-06-045 including Amendments thereto #1 and #2 with GlaxoSmithKline and FLU-06-086 with Kaketsuken should be terminated and any request asking for an amendment to the existing agreements need not be executed (see email from GSK below). Once the MTAs are terminated GSK and Kaketsuken will not be under any restrictions on use nor distribution of the Original Materials including any modified or unmodified derivatives.

I have attached a draft Agreement to Terminate letter for your review and consideration. Your concurrence with this proposed action via email by COB May 28th will be much appreciated. GSK and Kaketsuken have been waiting a resolution to this issue for quiet some time and I would very much like to provide them with this document.

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, May 28, 2009 1:19 PM
To: Watkins, Andrew (CDC/OD/OCSO); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Ok. I will draft the letter and send it to you for final "ok". GSK will be so happy!

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, May 28, 2009 11:18 AM
To: Knight, Janice (CDC/CCID/OD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

I don't see why not. It should do the trick nicely.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, May 28, 2009 7:43 AM
To: Watkins, Andrew (CDC/OD/OCSO); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1

Could I modify the above for use in terminating the MTAs for the reassortant viruses with GSK and Kaketsuken, Japan? Both companies have requested amendments to the original agreements to allow for their collaboration using the viruses and derivatives therefrom. I have tried to get resolution of this issue for some time and these 2 in particular wish answers.

Thanks so much,

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 5:22 PM
To: Knight, Janice (CDC/CCID/OD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Thanks. I would suggest the attached as a slightly different approach.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, May 27, 2009 4:54 PM
To: Watkins, Andrew (CDC/OD/OCSO); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

You should be able to use these.

JK

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 4:46 PM
To: Knight, Janice (CDC/CCID/OD); Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

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Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Would the attached documents be appropriate?

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 3:04 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Michael et al,

There is nothing in the agreements that requires us to renew and no reason to worry about liability. The companies received what they paid for. Not renewing a license that terminates naturally would not be considered a breach of the terms of the agreement. If it is your desire to make these materials publicly available for free and with no restrictions imposed by CDC, I believe you are free to do so.

However, it might be wise to send them a formal letter waiving the requirements of Paragraph 15, which requires them to destroy or return the materials upon termination of the license. I assume that would not be your intent in opening these materials to public use.

The companies should be delighted to be able to use the materials without obligation to pay monies, so I don't see a problem If they are not delighted, I still see no problem with not renewing the license. We have not agreed to do so anywhere in the agreement.

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Andrew,

Please find attached the executed BMLAs in question. "Natural Death" will occur mid to end of June 2009. LigoCyte is up to date on payments, Alphavax is slightly behind, but an Invoice has been issued to them.

Janice

Phone: 404 639-2679
FAX: 404 638-5465

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 2:06 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Michael,

I would like to see the agreements, but my first thought is that you can do what you want if the licenses are terminating by "natural death."

Andrew

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From: Shaw, Michael (CDC/CCID/NCIRD)
Sent: Wednesday, May 27, 2009 7:51 AM

To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Andrew,

We need some advice. We have been dropping all MTAs whenever possible on "live" virus but these licenses cover cDNA copies of virus genes created from HPAI isolates from Indonesia and Vietnam which, as you know, have been dealt with very carefully in the WHO/GISN negotiations on benefits and virus sharing. Both Nancy and I would prefer to drop them and let the companies deal with the countries themselves through the WHO Geneva office. This particular case is complicated by the fact that money has been received for past licensing fees. Would there be any liability for CDC if these were now dropped and the companies told they were on their own?

Janice can forward the documents if you'd like to examine them.

Michael

Michael W. Shaw, Ph.D.
Associate Director for Laboratory Science
Influenza Division, MS G-16
Centers for Disease Control and Prevention
Atlanta, GA 30333 USA

Tel.: (404)-639-1405
Fax: (404)-639-2350
Email: mws2@cdc.gov

From: Cox, Nancy (CDC/CCID/NCIRD)
Sent: Tuesday, May 26, 2009 6:44 PM
To: Shaw, Michael (CDC/CCID/NCIRD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

We may need to seek counsel from Andrew Watkins. I would prefer to drop and let them work it out with the countries but don't know for sure if that is best way forward.
N

From: Shaw, Michael (CDC/CCID/NCIRD)
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Importance: High

Nancy,

This case is not so obvious to me now that I know the details. This is for plasmid cDNA rather than the viruses themselves. Should we renew the licenses or drop them and have the companies pursue permission from Indonesia and Vietnam through WHO?

M

From: Knight, Janice (CDC/CCID/OD)
Sent: Tuesday, May 26, 2009 8:57 AM
To: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD)

Cc: Mawle, Alison (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Foster, Joseph A. (CDC/OCOO/OD); Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1
Importance: High

Mike just for clarification: Early in 2006 several regular (*i.e.,* not reverse genetics related) plasmids containing Indonesian and Vietnamese genetic material were licensed to LigoCyte Pharmaceuticals and Alphavax. Both agreements expire this year in June. Shall I inform both companies that they do not need to renew the license and that they may continue to use the materials (including any derivatives) with no restrictions?

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Subject: RE: Transfer of CDC Materials between parties to executed MTAs re H5N1

Janice,

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In light of the recent discussions among various CDC representatives from the Influenza Division, the National Center for Immunization and Respiratory Diseases, CCID Technology Transfer, the Office of General Counsel and the NIH Branch-HHS Office of the General Counsel, it would appear that the fully executed Material Transfer Agreements CDC Reference Numbers FLU-06-045 including Amendments thereto #1 and #2 with GlaxoSmithKline and FLU-06-086 with Kaketsuken should be terminated and any request asking for an amendment to the existing agreements need not be executed (see email from GSK below). Once the MTAs are terminated GSK and Kaketsuken will not be under any restrictions on use nor distribution of the Original Materials including any modified or unmodified derivatives.

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, May 28, 2009 11:12 AM
To: Lowenhaupt, Carol (CDC/CCID/OD) (CTR)
Cc: Watkins, Andrew (CDC/OD/OCSO); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: FW: Transfer of CDC Materials between parties to executed MTAs re H5N1
Attachments: Flu Termin Ltr Flu-06-052 Alphavax (3).aw.doc

Dear Carol,

Please use the letter attached for notification to LigoCyte. You will need to edit the document to contain the appropriate information pertaining to LigoCyte. Let me review before we send anything for Beth's signature as I will want to put various emails in the signature folder.

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Wednesday, May 27, 2009 5:22 PM
To: Knight, Janice (CDC/CCID/OD); Shaw, Michael (CDC/CCID/NCIRD)
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Influenza Division, MS G-16
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Regards,

Janice

Janice C. Knight

Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

[Out of Scope]

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, April 30, 2009 10:06 AM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD); Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Subject: RE: RE: Distribution of Influenza viruses

Importance: High

Ruben,

Do not share this email with anyone outside CDC. I have not received comments from Alison Mawle, Andrew Watkins and Joe Foster. Only Mike Shaw has responded so far. I do not know what the next step may be in publishing this policy if this is accepted as an accurate statement. Others will need to advise.

Janice

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Thursday, April 30, 2009 9:45 AM
To: Knight, Janice (CDC/CCID/OD)
Cc: Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD); Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Subject: RE: RE: Distribution of Influenza viruses

Janice,

Thanks this is very helpful –please let IFPMA know.

Can we summarize this into a brief policy statement? Such as (strawman):

CDC will distribute influenza viruses without any restrictions on use or further distribution; including 1) all influenza virus isolates of human, swine, and avian origin, as well as 2) all engineered reassortant viruses regardless of whether they are engineered using classical techniques or reverse genetics techniques.

Regarding << I have several pending amendments to existing agreements for the RG reassortants and need direction on how to proceed.>>

My suggestion would be for CDC to contact the requestors to let them know that an MTA will not be necessary and CDC will be providing the material as soon as possible.

Thanks,
Ruben

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, April 30, 2009 9:23 AM
To: Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD);

Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: RE: Distribution of Influenza viruses
Importance: High

Please respond to this email with your concurrence that the following statement reflects the official NCIRD policy on distribution of Influenza viruses:

No CDC influenza virus, other than the K9 isolate, will be transferred with any accompanying documentation containing any restrictions on use nor further distribution. The only documentation will be a package insert stating only that the material is provided as is with no warranties express or implied. The "influenza viruses" include the following:

1) all seasonal influenza virus isolates regardless of strain, *i.e.*, swine, human, avian etc. (excluding the K9 isolate under patent with outside entity)
2) all engineered reassortant viruses regardless of whether they are engineered using classical techniques or reverse genetics techniques

In light of the above statement, all MTAs having been executed to govern the transfer of the RG viruses by CDC, *i.e.*: 1) Influenza A virus reassortant Indo/05/2000(H5N1)/PR8-IBCDC-RG2; 2) Influenza A virus reassortant Viet/1203/2004(H5N1)/ PR8-IBCDC-RG; 3) Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG6 are no longer in effect and may be considered terminated. Any request asking for an amendment to the existing agreements need not be executed and the requestor may be informed that there are no longer any restrictions on use not distribution of any of these materials.

I have several pending amendments to existing agreements for the RG reassortants and need direction on how to proceed.

Thank you for your kind attention to this urgent matter.

Janice Knight
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, January 23, 2009 12:30 PM
To: Watkins, Andrew (CDC/OD/OCSO); Cox, Nancy (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD); Schuchat, Anne MD (CDC/CCID/NCIRD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: Distribution of Influenza viruses

I would like to summarize what I understand to be the current recommendation on the distribution of influenza viruses. No influenza virus, other than the K9 isolate, will be transferred with any accompanying documentation containing any restrictions on use nor further distribution. The only documentation will be a package insert stating only that the material is provided as is with no warranties express or implied. To this end I have drafted for your review a sample of what an insert might include. Please see attached. Perhaps in addition to this disclaimer, biosafety guidelines might be included where applicable.

Your comments may be reserved until the scheduled meeting on Jan 29.

Thank you,

Janice

Janice C. Knight

Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Shaw, Michael (CDC/CCID/NCIRD)
Sent: Thursday, April 30, 2009 9:24 AM
To: Knight, Janice (CDC/CCID/OD); Cox, Nancy (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: Re: RE: Distribution of Influenza viruses

That is correct.

From: Knight, Janice (CDC/CCID/OD)
To: Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Sent: Thu Apr 30 09:22:32 2009
Subject: RE: RE: Distribution of Influenza viruses
Please respond to this email with your concurrence that the following statement reflects the official NCIRD policy on distribution of Influenza viruses:

No CDC influenza virus, other than the K9 isolate, will be transferred with any accompanying documentation containing any restrictions on use nor further distribution. The only documentation will be a package insert stating only that the material is provided as is with no warranties express or implied. The "influenza viruses" include the following:

1) all seasonal influenza virus isolates regardless of strain, *i.e.*, swine, human, avian etc. (excluding the K9 isolate under patent with outside entity)
2) all engineered reassortant viruses regardless of whether they are engineered using classical techniques or reverse genetics techniques

In light of the above statement, all MTAs having been executed to govern the transfer of the RG viruses by CDC, *i.e.*: 1) Influenza A virus reassortant Indo/05/2000(H5N1)/PR8-IBCDC-RG2; 2) Influenza A virus reassortant Viet/1203/2004(H5N1)/ PR8-IBCDC-RG; 3) Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG6 are no longer in effect and may be considered terminated. Any request asking for an amendment to the existing agreements need not be executed and the requestor may be informed that there are no longer any restrictions on use not distribution of any of these materials.

I have several pending amendments to existing agreements for the RG reassortants and need direction on how to proceed.

Thank you for your kind attention to this urgent matter.

Janice Knight
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, January 23, 2009 12:30 PM
To: Watkins, Andrew (CDC/OD/OCSO); Cox, Nancy (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD); Schuchat, Anne MD (CDC/CCID/NCIRD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
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CONFIDENTIALITY NOTICE: This email and the attached document(s) may contain confidential information and may be otherwise protected by law. Its content should not be disclosed and it should not be given or copied to anyone other than the person(s) named or referenced above. If you have received this email in error, please contact the sender immediately.

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, April 30, 2009 9:23 AM
To: Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: RE: Distribution of Influenza viruses
Attachments: Package Insert-2009.doc

Importance: High

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I have several pending amendments to existing agreements for the RG reassortants and need direction on how to proceed.

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To: Watkins, Andrew (CDC/OD/OCSO); Cox, Nancy (CDC/CCID/NCIRD); Mawle, Alison (CDC/CCID/NCIRD); Schuchat, Anne MD (CDC/CCID/NCIRD)
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1. THE MATERIALS ARE BEING SUPPLIED WITH NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

2. Recipient is encouraged to publish the results of any research in scientific publications and the contribution of CDC, unless requested otherwise by CDC.

3. The Materials may pose health risks to laboratory workers, the community, and the environment; therefore, the appropriate biosafety standards including special practices, equipment and facilities as necessary shall be employed. All applicable Recipient and Government health and safety regulations shall be followed.

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Hoelscher, Mary (CDC/CCID/NCIRD)
Sent: Tuesday, March 31, 2009 11:32 AM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Villanueva, Julie M. (CDC/CCID/NCIRD) (CTR)
Subject: RE: H5viruses

Andrew,

Might you have some time to chat briefly by con call to discuss what we need to complete the documents (per the TTO side of things) to get a process in place as requested by Alison for the Center? Alison would like the policy to be comprehensive in anticipation for issues with the rest of CDC as others might start questioning why they have to deal with MTAs. I am holding several requests for the reassortants and plasmids until we have a process and SOP in place. Thanks

Mary

From: Villanueva, Julie M. (CDC/CCID/NCIRD) (CTR)
Sent: Wednesday, March 25, 2009 10:03 AM
To: Hoelscher, Mary (CDC/CCID/NCIRD); Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: H5viruses

Hello Andrew,

I have been asked by Mary Hoelscher and Alison Mawle to assist with the writing of a new policy/SOP for the Influenza Division for H5 virus requests. I was hoping to speak with you regarding the email chain below that discusses the IP issues surrounding the vaccine candidate H5 reassortant viruses created by Rubin Donis' group. Is it possible to arrange some time to discuss this matter?

Thank you so much for your time,
Julie Villanueva

Julie Villanueva, Ph.D., PMP
Program Manager / Battelle (CTR)
Centers for Disease Control and Prevention
CCID/NCIRD/Influenza Division
1600 Clifton Road NE, MS G-03
Atlanta, GA 30333
404-639-3851
JVillanueva@cdc.gov

From: Hoelscher, Mary (CDC/CCID/NCIRD)
Sent: Monday, March 23, 2009 11:00 AM
To: Villanueva, Julie M. (CDC/CCID/NCIRD) (CTR)
Subject: FW: H5viruses

For tomorrow's meeting with Alison.

From: George Brownlee [mailto:george.brownlee@path.ox.ac.uk]
Sent: Monday, March 23, 2009 11:08 AM
To: Cox, Nancy (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD)
Cc: Hoelscher, Mary (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); 'Ervin Fodor'
Subject: RE: H5viruses

Dear Nancy and Ervin,
I have modified your proposed letter (see attachment) slightly to delete the statement that your modificantion to our plasmids is a significant IP modification; I cannot judge that in terms of IP input - that is for the lawyers to decide. Instead, I inserted the precedent (next paragraph) set by the Wood lab which, as far as I am concerned, was a prime reason for my agreeing that your laboratory could distribute the candidate vaccine strains, subject to any IP matters being discussed with (b)(4)

With kind regards,
George

From: Cox, Nancy (CDC/CCID/NCIRD) [mailto:njc1@cdc.gov]
Sent: 22 March 2009 14:31
To: george.brownlee@path.ox.ac.uk; Donis, Ruben O. (CDC/CCID/NCIRD)
Cc: Hoelscher, Mary (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD)
Subject: FW: H5viruses

Dear George,

Thank you again for your discussion and for your agreement for us to distribute seed rg H5N1 viruses that are suitable as potential vaccine viruses without an MTA limiting their use. I have been asked by our technology transfer staff to ask you to read what I have written below and indicate that you agree with it or if there are any restrictions on our distributing such rg vaccine candidates.

I am sorry for the inconvenience and thank you for your collaboration and cooperation over many years. Please let us know at your earliest convenience.

Sincerely,
Nancy

From: Cox, Nancy J. (CDC)
Sent: Thursday, March 05, 2009 1:16 PM
To: Watkins, Andrew C. (CDC); Hoelscher, Mary A. (CDC); Shaw, Michael W. (CDC); Donis, Ruben (CDC); Miller, Joseph (CDC); Jernigan, Daniel B. (CDC); Berkley, Dale (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]
Cc: Miller, Daniel S (OS)
Subject: FW: H5viruses

Andrew and All,

Ruben Donis and I phoned Dr. George Brownlee yesterday morning to discuss whether or not we needed and MTA to send out the rg viruses made using the CDC modified Oxford University plasmids that were received from them. We explained that we had used their 12 plasmid system and had modified the ends of the relevant plasmids so as to convert their 12 plasmid system to a 8 plasmid system. He agreed that CDC had put a substantial amount of IP into the modifications.

He stated that we are free to send out the rg viruses made with the modified Oxford plasmids without an MTA. Therefore, I believe we have the go ahead to send out the rg candidate vaccine viruses using the disclaimer form that states that the end user is responsible for "taking care of IP inherent in the material" , proper biosafety and all the rest.

Below is the e-mail he sent after he spoke with his Oxford colleagues who were also involved with making the original Oxford 12 plasmids for reverse genetics of influenza viruses. Oxford's IP is now under (b)(4) so I think that this all fits together nicely. Please call me if you have any questions.

Thanks,
Nancy

From: George Brownlee [mailto:george.brownlee@path.ox.ac.uk]
Sent: Wednesday, March 04, 2009 9:33 AM
To: Cox, Nancy (CDC/CCID/NCIRD)
Cc: 'Ervin Fodor'
Subject: H5viruses

Dear Nancy,
Following our telephone discussion this morning, we agree to the course of action you propose i.e. to distribute seed H5N1 viruses suitable as potential vaccine strains.
With kind regards,
George G Brownlee

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Lindstrom, Stephen (CDC/CCID/NCIRD)
Sent: Monday, March 16, 2009 2:08 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Candal, Francisco (Paco) (CDC/OD/OCSO)
Subject: RE: Taqman IP

Hi Andrew,
Thanks for the background. It looks like the main patent is the following:

http://patft.uspto.gov/netacgi/nph-Parser?Sect2=PTO1&Sect2=HITOFF&p=1&u=%2Fnetahtml%2FPTO%2Fsearch-bool.html&r=1&f=G&l=50&d=PALL&RefSrch=yes&Query=PN%2F5723591

United States Patent **5,723,591**
Livak , et al. **March 3, 1998**

Self-quenching fluorescence probe

Abstract

An oligonucleotide probe is provided which includes a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of the reporter molecule. The oligonucleotide probe is constructed such that the probe exists in at least one single-stranded conformation when unhybridized where the quencher molecule is near enough to the reporter molecule to quench the fluorescence of the reporter molecule. The oligonucleotide probe also exists in at least one conformation when hybridized to a target polynucleotide where the quencher molecule is not positioned close enough to the reporter molecule to quench the fluorescence of the reporter molecule. By adopting these hybridized and unhybridized conformations, the reporter molecule and quencher molecule on the probe exhibit different fluorescence signal intensities when the probe is hybridized and unhybridized. As a result, it is possible to determine whether the probe is hybridized or unhybridized based on a change in the fluorescence intensity of the reporter molecule, the quencher molecule, or a combination thereof. In addition, because the probe can be designed such that the quencher molecule quenches the reporter molecule when the probe is not hybridized, the probe can be designed such that the reporter molecule exhibits limited fluorescence until the probe is either hybridized or digested.

There are a number of associated patents and reference listed on the same page.

Thank you!
Steve

****
Stephen Lindstrom, Ph.D.
Team Lead, Diagnostics Development Team
Virus Surveillance and Diagnosis Branch
Influenza Division, NCIRD
Centers for Disease Control and Prevention
1600 Clifton Road NE Atlanta, GA 30333
Phone: 404-639-1587
Fax: 404-639-0080
****

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Monday, March 16, 2009 1:13 PM

To: Lindstrom, Stephen (CDC/CCID/NCIRD)
Cc: Candal, Francisco (Paco) (CDC/OD/OCSO)
Subject: RE: Taqman IP

Steve,

Do you know which patents cover the Taqman IP? It would save us from searching, perhaps ineffectively, if you already have the patent numbers.

You are asking complicated questions, but here goes my attempt at simple (ha) answers.

The short answer to question 1 is yes, we could possibly be accused of infringing depending on the actual circumstances. For example if we are distributing taqman test reagents knowing that use in the patented method is their only purpose, then it might be possible that the user would be infringing the patent and we might possibly be accused of being "contributory infringers." True or not I am not willing to weigh in on just yet.

Second question will depend on finding out if federal funds were used to make the invention. If so, the government would have "government use rights," but there is some controversy over how far and to whom those use rights extend.

First step is to find out if Federal funding was used.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Lindstrom, Stephen (CDC/CCID/NCIRD)
Sent: Friday, March 13, 2009 5:34 PM
To: Candal, Francisco (Paco) (CDC/OD/OCSO)
Cc: Watkins, Andrew (CDC/OD/OCSO)
Subject: Taqman IP

Hi Paco,
I was wondering if we could get TTO's take on an issue that has come up regarding licensing of Taqman IP from AB and/or Roche. The question is regarding if either company could make a claim that CDC is infringing on their IP by distributing taqman test reagents for free that may be taking market share away from those companies. After the meeting with AB where IP licensing was discussed, some folks at CDC are now a little nervous about putting CDC in a situation where the US gov't could be sued.

A similar issue came up with use and distribution of vaccine strains generated using reverse genetics techniques. A critical question came down to if this IP was developed from US government grant money. Reverse genetics was developed under NIH funding, so the US government is not required pay licensing fees on this IP.
Is it possible to find out if IP/patents associated with the Taqman IP were originally developed US government funding? If this is the case, I suspect that the grants/contract would have been between either DoD or NIH and Idaho Technologies and/or Roche.

I'm happy to talk with you and Andrew about this question and possible options.

Thank you.
Steve

****
Stephen Lindstrom, Ph.D.
Team Lead, Diagnostics Development Team
Virus Surveillance and Diagnosis Branch
Influenza Division, NCIRD

Centers for Disease Control and Prevention
1600 Clifton Road NE Atlanta, GA 30333
Phone: 404-639-1587
Fax: 404-639-0080
****

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, March 06, 2009 9:46 AM
To: Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: H5viruses

Andrew, this is you day off remember? So go sit outside in the sun and chill out. Life is short and our sun time is limited. Cogent and concise advice from the sage.

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Friday, March 06, 2009 8:41 AM
To: Knight, Janice (CDC/CCID/OD)
Subject: RE: H5viruses

I think the short and to the point is a wise move. That reminds me of the Intro to Political Science course I took as a Freshman in college. I breezed through the high school in my little lower middle class urban town, and had a rude awakening when I got to college. On the final exam for the poli sci course, the instructions for the essay answers was to be certain to make your answers "cogent and concise." Being from a town where everyone scraped by to survive, we weren't real big on fancy words. I had no idea what either of those words meant and the professor would not give definitions. What a nightmare that test was. I got my first and last "D" grade, partly from not knowing what those words meant. I learned that lesson well.

So, what caused that diversion is that what you are proposing to do, of course, is to make the label language "cogent and concise."

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, March 06, 2009 8:35 AM
To: Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: H5viruses

Thanks for the suggestion, I do like the way both sentences read and will definitely incorporate one or the other. I am going to try to keep it short and to the point in order to avoid as much confusion as possible.

JK

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, March 05, 2009 4:38 PM
To: Knight, Janice (CDC/CCID/OD)
Subject: RE: H5viruses

I'm sure I saw satisfactory disclaimer of liability label language recently. The other issue I'm not sure we even need to address but if we do, let me think. I would start with something like this:

"It is the responsibility of the recipient to determine if there are any patents that may block use of the material in commerce." or "It is the responsibility of the recipient to obtain any licenses to intellectual property that may be required for use of the material in commerce."

I hope that helps.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, March 05, 2009 4:28 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: H5viruses

No, we really didn't have much going. I think they had used a modification of the User Fee Letter, but weren't happy with the restrictions in it. I will probably start with that and work with Mary Hoelscher to get a good draft that meets what Flu wants it to say. We have had so many discussions that I get confused, so I want to work on this closely with Mary before I put is out for everyone to critique. I assume we will have to get some clearance on this above the Division level???

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, March 05, 2009 4:23 PM
To: Knight, Janice (CDC/CCID/OD)
Subject: RE: H5viruses

Oops, I thought you already had something. I remember reading a draft of some label language, seems like a month or so ago. Was that Lisa's? I am happy to help but what do you want help with?

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, March 05, 2009 4:20 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: H5viruses

Whoa there nellie, when did this happen? I thought you were going to draft this document! Oh well, as they say stuff rolls downhill. I will work on a rough draft tomorrow and try to get it together for review maybe Monday. Maybe we can add this to my list of "Issues" to discuss during the call Monday if you are available.

Happy Friday off-

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, March 05, 2009 3:54 PM
To: Hoelscher, Mary (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Miller, Joseph D. (CDC/CCID/NCIRD); Jernigan, Daniel B. (CDC/CCID/NCIRD); Blake-

DiSpigna, Lisa (CDC/CCID/OD); Knight, Janice (CDC/CCID/OD)
Cc: Miller, Daniel S.(HHS/OGHA)
Subject: RE: H5viruses

I believe the ball is now back in Lisa Blake-Dispigna's teams' court, specifically Janice Knight. I am happy to help any way I can.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Hoelscher, Mary (CDC/CCID/NCIRD)
Sent: Thursday, March 05, 2009 3:07 PM
To: Watkins, Andrew (CDC/OD/OCSO); Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Miller, Joseph D. (CDC/CCID/NCIRD); Jernigan, Daniel B. (CDC/CCID/NCIRD)
Cc: Miller, Daniel S.(HHS/OGHA)
Subject: RE: H5viruses

So we can now move forward on the disclaimer to be included with the reassortants. Should we only have one disclaimer to cover wild type and reassortant viruses with mention of the responsibility of IP issues be the sole responsibility of the recipient of the viruses?

Andrew, can we help with anything on this? Did I forward the current disclaimer for the seasonal viruses?

Mary

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, March 05, 2009 1:48 PM
To: Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Miller, Joseph D. (CDC/CCID/NCIRD); Jernigan, Daniel B. (CDC/CCID/NCIRD); Berkley, Dale (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]
Cc: Miller, Daniel S.(HHS/OGHA)
Subject: RE: H5viruses

That's great news. Thanks. That will remove what I believe to be the last roadblock. Wonderful.

Andrew

Andrew Watkins
Director, CDC Technology Transfer Office

From: Cox, Nancy (CDC/CCID/NCIRD)
Sent: Thursday, March 05, 2009 1:16 PM
To: Watkins, Andrew (CDC/OD/OCSO); Hoelscher, Mary (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Miller, Joseph D. (CDC/CCID/NCIRD); Jernigan, Daniel B. (CDC/CCID/NCIRD); Berkley, Dale (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]
Cc: Miller, Daniel S.(HHS/OGHA)
Subject: FW: H5viruses

Andrew and All,

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Thanks,
Nancy

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Sent: Wednesday, March 04, 2009 9:33 AM
To: Cox, Nancy (CDC/CCID/NCIRD)
Cc: 'Ervin Fodor'
Subject: H5viruses

Dear Nancy,
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With kind regards,
George G Brownlee

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, March 05, 2009 4:31 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: H5viruses

Yes, we do need help, but unless some miracle happens, I don't see it in the near future!

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, March 05, 2009 4:24 PM
To: Knight, Janice (CDC/CCID/OD)
Subject: RE: H5viruses

Friday off???? I can no longer remember the last time that happened. Lately, I haven't even had the luxury of at least working from home in comfortable jeans. We need help!!!!!!

Andrew Watkins
Director, CDC Technology Transfer Office

From: Knight, Janice (CDC/CCID/OD)
Sent: Thursday, March 05, 2009 4:20 PM
To: Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: H5viruses

Whoa there nellie, when did this happen? I thought you were going to draft this document! Oh well, as they say stuff rolls downhill. I will work on a rough draft tomorrow and try to get it together for review maybe Monday. Maybe we can add this to my list of "Issues" to discuss during the call Monday if you are available.

Happy Friday off-

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, March 05, 2009 3:54 PM
To: Hoelscher, Mary (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Miller, Joseph D. (CDC/CCID/NCIRD); Jernigan, Daniel B. (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD); Knight, Janice (CDC/CCID/OD)
Cc: Miller, Daniel S.(HHS/OGHA)
Subject: RE: H5viruses

I believe the ball is now back in Lisa Blake-Dispigna's teams' court, specifically Janice Knight. I am happy to help any way I can.

Andrew Watkins
Director, CDC Technology Transfer Office

From: Hoelscher, Mary (CDC/CCID/NCIRD)
Sent: Thursday, March 05, 2009 3:07 PM
To: Watkins, Andrew (CDC/OD/OCSO); Cox, Nancy (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Miller, Joseph D. (CDC/CCID/NCIRD); Jernigan, Daniel B. (CDC/CCID/NCIRD)
Cc: Miller, Daniel S.(HHS/OGHA)
Subject: RE: H5viruses

So we can now move forward on the disclaimer to be included with the reassortants. Should we only have one disclaimer to cover wild type and reassortant viruses with mention of the responsibility of IP issues be the sole responsibility of the recipient of the viruses?

Andrew, can we help with anything on this? Did I forward the current disclaimer for the seasonal viruses?

Mary

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Thursday, March 05, 2009 1:48 PM
To: Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Miller, Joseph D. (CDC/CCID/NCIRD); Jernigan, Daniel B. (CDC/CCID/NCIRD); Berkley, Dale (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]
Cc: Miller, Daniel S.(HHS/OGHA)
Subject: RE: H5viruses

That's great news. Thanks. That will remove what I believe to be the last roadblock. Wonderful.

Andrew

Andrew Watkins
Director, CDC Technology Transfer Office

From: Cox, Nancy (CDC/CCID/NCIRD)
Sent: Thursday, March 05, 2009 1:16 PM
To: Watkins, Andrew (CDC/OD/OCSO); Hoelscher, Mary (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Miller, Joseph D. (CDC/CCID/NCIRD); Jernigan, Daniel B. (CDC/CCID/NCIRD); Berkley, Dale (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]
Cc: Miller, Daniel S.(HHS/OGHA)
Subject: FW: H5viruses

Andrew and All,

Ruben Donis and I phoned Dr. George Brownlee yesterday morning to discuss whether or not we needed and MTA to send out the rg viruses made using the CDC modified Oxford University plasmids that were received from them. We explained that we had used their 12 plasmid system and had modified the ends of the relevant plasmids so as to convert their 12 plasmid system to a 8 plasmid system. He agreed that CDC had put a substantial amount of IP into the modifications.

He stated that we are free to send out the rg viruses made with the modified Oxford plasmids without an MTA. Therefore, I believe we have the go ahead to send out the rg candidate vaccine viruses using the disclaimer form that states that the end user is responsible for "taking care of IP inherent in the material" . proper biosafety and all the rest.

Below is the e-mail he sent after he spoke with his Oxford colleagues who were also involved with making the original Oxford 12 plasmids for reverse genetics of influenza viruses. Oxford's IP is now under (b)(4) so I think that this all fits together nicely. Please call me if you have any questions.

Thanks,
Nancy

From: George Brownlee [mailto:george.brownlee@path.ox.ac.uk]
Sent: Wednesday, March 04, 2009 9:33 AM
To: Cox, Nancy (CDC/CCID/NCIRD)
Cc: 'Ervin Fodor'
Subject: H5viruses

Dear Nancy,
Following our telephone discussion this morning, we agree to the course of action you propose i.e. to distribute seed H5N1 viruses suitable as potential vaccine strains.
With kind regards,
George G Brownlee

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Monday, January 12, 2009 9:54 AM
To: Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); McNeill, Valerie (CDC/CCID/OD) (CTR)
Subject: RE: MTA

Andrew,

Thank you so much for taking time out to discuss the influenza issues with me this morning. I just want to confirm with you that I understood things. As I recall you are going to set up a committee comprised of individuals with the appropriate authority to revisit the terms and conditions for distribution of the influenza viruses including the reverse genetics derived reassortants (RG reassortant) with emphasis on commercial use as well as development. In the meantime, we are to hold those requests for the various RG reassortant viruses that come in on the Pre-approved template until we get clearance from you as to the appropriate language to use to govern these transfers. I hope we can now get everyone to make a concrete decision on exactly what is the appropriate language to govern these transfers. Here is a list of the program/division individuals that might be considered for participation:

Ruben Donis
Mike Shaw or Dan Jernigan or Nancy Cox
Alison Mawle

And of course, Lisa and I would certainly like to be present as a silent observers.

As ever,

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Sunday, January 11, 2009 1:02 PM
To: Cox, Nancy (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Berkley, Dale (NIH/OD) [E]
Cc: Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

Folks,

I am in agreement with Ruben and Nancy's sentiments. During the course of our many discussions about influenza vaccine virus transfers, I believe we concluded that as long as the current system of transferring our standard vaccine virus candidates to vaccine manufacturers is successful, and neither requires nor would benefit substantially from the use of our formal technology transfer tools, then we should continue the approach that has worked for several decades. This, especially in light of the international concerns over use of influenza viruses obtained originally from sensitive countries, unless by licensing the viruses we can better ensure equitable distribution to those counties. Is that a role we wish to take on here?

At the same time, we must also make certain that we are not violating anyone else's legitimate rights or any obligations we have made to others. I believe we are past that point with (b)(4) (AstraZeneca) at this point, provided we ensure that we make those rights clear to companies or other entities to which we transfer the viruses, as Janice has noted quite well.

In my opinion, and consistent with our many discussions, we should find a way to remove the restrictions on use of the reassortants, while ensuring we are clear about any restrictions that may be imposed by others, but we should get out of the middle of those rights as best we can.

I will need to see Tim Howe's markup of our Letter Agreement - it did not come through with this email chain. Ruben, Janice, can one of you please forward that to me?

Thanks,
Andrew

Andrew Watkins
Director, CDC Technology Transfer Office

From: Cox, Nancy (CDC/CCID/NCIRD)
Sent: Saturday, January 10, 2009 4:29 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Berkley, Dale (NIH/OD) [E]
Cc: Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

Janice,

More food for thought.

1. We have had many, many discussions about these matters leading up to the Intergovernmental Meeting held last December. NIH lawyer Dale Berkeley is very much aligned with us in our approach and I have copied him here.

2. We have **never** received royalties for any of the influenza viruses provided to vaccine manufacturers for vaccine manufacture during my entire tenure at CDC which is just over 33 years. If I am wrong someone please correct me.

3. Influenza B viruses used in influenza vaccines are almost always wild-type viruses and we provide them free of charge throughout the WHO system and to vaccine manufacturers on an annual basis, no strings attached.

4. Seasonal influenza A viruses provided to vaccine manufacturers are typically high growth reassortants that are produced by specialized laboratories but no royalties go to the country of origin, to the WHO or the experts that make the vaccine strain selection and provide the viruses to the specialized labs to make the high growth reassortants, nor to the specialized labs that make the seasonal high growth reassortants. The work has to be done very quickly to meet very short timelines and we try to streamline every step.

5. We backed ourselves into a corner with the old MTA and now we are trying to get out. Please help.

Thanks,
Nancy

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Friday, January 09, 2009 5:41 PM
To: Knight, Janice (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

All,

If I may, I will wear my intergalactic observer hat for a moment and make some comments:

1. CDC has access to many of the influenza viruses used in the derivation of reassortants by reverse genetics through its role as WHO Collaborating Center; therefore CDC is not the sole "owner" of said reassortants.

2. CDC's mission is to reduce influenza mortality and morbidity; the best way to do this is by global vaccination and ~90% the vaccine used worldwide is produced by pharmaceutical companies.

3. Vaccine manufacturing is a high risk business proposition: most big pharmas are very cautious about investing in vaccine product development (it may get worse before it gets better).

4. For example, in 2006-2007 HHS gave $1 billion to 4 vaccine companies (no typos here, yes this is a done deal) to promote development of influenza vaccine manufacturing capacity in the continental USA.

5. To promote #2 and address #3, CDC makes the candidate vaccine strains and distributes them free of charge globally to encourage companies to develop and manufacture vaccines to immunize people.

6. CDC should not try to collect royalties for the seasonal or pandemic influenza vaccine candidates because we do not contribute intellectual property and also because it counters what HHS wanted to accomplish under #4 and #5.

7. CDC transfers the material to companies worldwide and informs the recipient that the material was produced using a proprietary technology and they are responsible for not violating the law with the use of the material. Doing otherwise would entail CDC taking on an IP enforcement role.

8. If vaccine companies can make money selling influenza vaccines, this may translate into more and better vaccines, which will help accomplish CDC's mission. Win-win situation. Vaccine companies may have to pay royalties to the owners of the IP (be it (b)(4) St Jude, etc), it is not for CDC to sort that out. Let US-DOJ or US-DOC deal with such IP issues.

9. The main concern for CDC should be to liability: we do not want to be liable for anything as a result of giving a vaccine candidate to a Company.

What risks would CDC face by distributing vaccine candidates under a rather liberal MTA? Would such risks outweigh the substantial benefits?

Thanks,
Ruben

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, January 09, 2009 3:40 PM
To: Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: FW: MTA

All,

I have reviewed the documents from Sanofi Pasteur attached to the email below and I have some thoughts. The edited draft of the CDC Letter Agreement seems to me to give Sanofi unlimited commercialization rights and would exclude CDC from receiving any royalty on CDC's IP in the RG Reassortants. Granted they have a license from AstraZeneca, but what does CDC do about licensure of these viruses? Are we going to provide these materials for commercial sale without any license agreement and no royalties of any sort? I reviewed the 2008 NIBSC agreement and I am not clear what Article 6.2 grants. Is NIBSC giving Sanofi all IP in modifications and all derivatives? Would this be granting rights is advance, which I thought CDC didn't do? Article 6.3 restricts use of the original materials from commercialization, but does not address IP that might remain within a modification or derivative.

Bottom line is under what terms does CDC allow commercialization of the RG Reassortants? I have attached blank templates of the Biological Materials License Agreement (BMLA) and my most current copy of the Proprietary Technology License Agreement (PTLA) for your information. In addition, in the BMLA we have used the following addition where provision by the commercial Licensee to developing countries was applicable:

*" d. An earned royalty that will be reduced to one half percent (0.5%) of **Net Sales** on **Licensed Products** sold in countries classified as low-income and lower-middle-income economies by the World Bank (www.worldbank.org). Classification will be reassessed at the beginning of each calendar year. "*

Janice

Janice C. Knight

Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Wednesday, January 07, 2009 5:37 PM
To: Miller, Daniel S.(HHS/OGHA); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO)
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: FW: MTA

All,

It has been a few years since development of the terms of the MTA (or Simple Letter of Agreement) under which candidate vaccine strains prepared at CDC using reverse genetics technology have been distributed to vaccine manufacturers. As you know, the IP landscape of influenza reverse genetics has changed in the recent past: (b)(4) has negotiated licenses with several vaccine companies to use this technology. I am receiving requests from these companies to revisit the terms of the MTA/SLA for future pandemic vaccine strains (and even retroactively). I am attaching a copy on one such request as an example. It is in the best interest of HHS to enable the proposed activities regarding pandemic vaccines: "internal research and development as well as in clinical trials, product development, licensure, donation and commercialization". Sanofi claims to have worked out MTA with our counterpart in the UK (NIBSC) that allows them to do all these things (see attached document).

HHS may not want to change anything, or perhaps some favorable conditions could be granted. In any case, re-evaluating the MTA/SLA and establishing consensus on the course of action would be important to be able to respond to the requests from companies. Please let me know how you would like to proceed; i.e. teleconference, face to face meeting, who else needs to be involved and so on.

Best regards,

Ruben

Ruben Donis, PhD

Chief, Molecular Virology and Vaccines Branch
Influenza Division, NCIRD, CCID
Centers for Disease Control and Prevention
1600 Clifton Road - Mail Stop G-16
Atlanta, GA 30333
Phone: (404) 639-4968
Fax: (404) 639-2350

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Wednesday, January 07, 2009 3:45 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: RE: MTA

Hi Ruben, Here is what we have come up with.

We received material from CDC under the form of Letter Agreement that you provided. On its face the agreement restricts our use of material to activities in furtherance of a specific contract with HHS. We want to amend the letter agreement(s), with retroactive effect, to allow us to engage in internal research and development as well as in clinical trials, product development, licensure, donation and commercialization. As you may know, (b)(4) (now AstraZeneca) consolidated all of the IP rights related to reverse genetics and plasmid rescue and offered these rights up as a license package. We took a non-exclusive license from (b)(4) and that is a matter of public record. You can google for the press release that (b)(4) made. (they subsequently signed up most, if not all, of the other players). Alternatively, I would invite you to contact Mr. Atul Saran, Esq., Sr. Director and Secretary of (b)(4) He will be happy to confirm that we took a license, and I'm sure he will be willing to facilitate the proposed agreement between CDC and sanofi pasteur, as the license from (b)(4) to (b)(4) He can be reached at: (301) 398-4759. We could also provide you with redacted copies of our license agreements, if that would help.

According to the terms of our agreements with (b)(4) we can do whatever we want with material derived from RG/plasmid rescue, and can practice such methods ourselves, except that we can't make NS-1 modifications, can't work with the A/Ann Arbor backbone, and can't make live, attenuated flu. We don't have any intention of doing any of these things.

One of our attorneys here, Tim Howe, took your draft letter agreement and made some modifications. His draft is attached as mark-up. He plans next to prepare a draft amendment to the existing agreements as an alternative to this approach, but if this form of Letter Agreement is satisfactory to CDC it will work for us.

So, if we understand correctly, CDC simply wanted to be sure that any recipient of these materials would respect the IP rights of third parties. We are doing that, and can amply document that. Hopefully that means we can move ahead quickly now to secure the rights we need to continue in our efforts towards pandemic preparedness.

Thank you, as always, for your help in these matters.

Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,
Swiftwater, PA.18370
570-957-2513

From: Donis, Ruben O. (CDC/CCID/NCIRD) [mailto:rvd6@cdc.gov]
Sent: Friday, November 28, 2008 1:09 PM
To: Hjorth, Richard (sanofi pasteur)
Subject: RE: MTA

Richard,
Please see the below generic Simple Letter Agreement and let me know what changes would be desirable for Sanofi.
I just want to be sure I am on the same page when this is brought to the attention of HHS.
Thanks,
Ruben

Letter Agreement
In response to the request of COMPANY X, Inc. ("RECIPIENT") made to the Centers for Disease Control and Prevention ("PROVIDER') to be provided with the Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG6 Reference Strain ("MATERIAL") possessed by the PROVIDER" the PROVIDER asks that the RECIPIENT agee to the following before the RECIPIENT receives the MATERIAL:

The MATERIAL will be used in accordance with the following contract which RECIPIENT has been awarded by US Department of Health and Human Services: HHSOxxxx. The MATERIAL will be used by the RECIPIENT for the purpose of the research, development and manufacture of influenza vaccines for US Department of Health and Human Services. Commercialization of the MATERIAL or vaccine derived from the MATERIAL may require commercialization licenses from extant patent holder(s) of the reverse genetics methodology andlor products obtained using reverse genetics methods.

With the exception of the distribution of the MATERIAL and vaccine derived from the MATERIAL (a) among the RECIPIENT's (or its affiliates') facilities and operations in xxxx(b) to the US Department of Health and Human Services,
which the PROVIDER hereby consents to, the MATERIAL will not be further distributed by the RECIPIENT without the PROVIDER's written consent. The RECIPIENT shall refer to the PROVIDER any request for the MATERIAL by any individual or company outside of the RECIPIENT and its affiliates.

Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. THE PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Unless prohibited by law, the RECIPIENT assumes all liability for claims for damages.

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Wednesday, November 26, 2008 3:05 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: RE: MTA

Thanks for the quick follow up. Tim is excited about this. Here's a note from him: All my contact has been with Janice Knight in Tech Transfer. She's spoken with their OGC but I have not.

While I'm at it, in anticipation of a successful resolution of the dilemna and perhaps as a test case would you be willing to ship us your A/Chicken/India/NIV33407/2006? Also, the list we saw said the FDA had A/Duck/Laos/3295/2006. I didn't think FDA made these. Is this yours?

(b)(4)

Thanks again,
Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,
Swiftwater, PA.18370
570-957-2513

From: Donis, Ruben O. (CDC/CCID/NCIRD)
To: 'Richard.Hjorth@sanofipasteur.com'
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD)
Sent: Tue Nov 25 22:42:15 2008
Subject: FW: MTA

Hi Richard,
I see your point. I think we are moving towards CDC providing rg-derived vaccine candidates to manufacturers without any use restrictions – CDC will simply ask for waivers of liability and inform recipients that they are reponsible for compliance with IP laws.

I am copying Michael Shaw and Nancy Cox who have been in discussions about updating the MTA – not sure if the CDC legal folks are going to embrace this liberal approach.

Best regards,
Ruben

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Tuesday, November 25, 2008 10:11 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: FW: MTA

Hi Ruben,
I wonder if I can enlist your help with a mutually beneficial endeavor. One of our senior lawyers, Tim Howe, has been trying to work on this with some CDC lawyers and they don't seem to be getting very far. The issue is that you are making pre-pandemic vaccine viruses but right now, there are too many restrictions on their use in the CDC Simple Letter Agreements for them to be of much use to us. We would like to be able to use these strains to make commercial vaccines and to make donations to WHO. We've already commited as a company to donate to WHO.
We already have worked out an agreement with (b)(4) that allows us to do all these things. Perhaps this could be a model for a similar CDC agreement.
I am hoping you might know the right people to speak with that may be able to move this along. I would hate to have to ask the NIBSC to make the same viruses you have already made just so we can use them. As you know, we already have an agreement with (b)(4) use their reverse genetics so that should not be a concern.
Thanks for any help you can provide,
Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,

Swiftwater, PA.18370
570-957-2513

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Sunday, January 11, 2009 2:51 PM
To: Watkins, Andrew (CDC/OD/OCSO); Cox, Nancy (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Berkley, Dale (NIH/OD) [E]
Cc: Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA
Attachments: MTANIBSC2008.pdf; MTANIBSC2007.pdf; draft CDC Letter Agreement (markup).doc

Thanks Andrew, great to hear that there may be consensus on way forward.
The draft from Sanofi is attached.
Best,
Ruben

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Sunday, January 11, 2009 1:02 PM
To: Cox, Nancy (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Berkley, Dale (NIH/OD) [E]
Cc: Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

Folks,

I am in agreement with Ruben and Nancy's sentiments. During the course of our many discussions about influenza vaccine virus transfers, I believe we concluded that as long as the current system of transferring our standard vaccine virus candidates to vaccine manufacturers is successful, and neither requires nor would benefit substantially from the use of our formal technology transfer tools, then we should continue the approach that has worked for several decades. This, especially in light of the international concerns over use of influenza viruses obtained originally from sensitive countries, unless by licensing the viruses we can better ensure equitable distribution to those counties. Is that a role we wish to take on here?

At the same time, we must also make certain that we are not violating anyone else's legitimate rights or any obligations we have made to others. I believe we are past that point with (b)(4) at this point, provided we ensure that we make those rights clear to companies or other entities to which we transfer the viruses, as Janice has noted quite well.

In my opinion, and consistent with our many discussions, we should find a way to remove the restrictions on use of the reassortants, while ensuring we are clear about any restrictions that may be imposed by others, but we should get out of the middle of those rights as best we can.

I will need to see Tim Howe's markup of our Letter Agreement - it did not come through with this email chain. Ruben, Janice, can one of you please forward that to me?

Thanks,
Andrew

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Director, CDC Technology Transfer Office

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Sent: Saturday, January 10, 2009 4:29 PM
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Cc: Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

Janice,

More food for thought.

1. We have had many, many discussions about these matters leading up to the Intergovernmental Meeting held last December. NIH lawyer Dale Berkeley is very much aligned with us in our approach and I have copied him here.

2. We have **never** received royalties for any of the influenza viruses provided to vaccine manufacturers for vaccine manufacture during my entire tenure at CDC which is just over 33 years. If I am wrong someone please correct me.

3. Influenza B viruses used in influenza vaccines are almost always wild-type viruses and we provide them free of charge throughout the WHO system and to vaccine manufacturers on an annual basis, no strings attached.

4. Seasonal influenza A viruses provided to vaccine manufacturers are typically high growth reassortants that are produced by specialized laboratories but no royalties go to the country of origin, to the WHO or the experts that make the vaccine strain selection and provide the viruses to the specialized labs to make the high growth reassortants, nor to the specialized labs that make the seasonal high growth reassortants. The work has to be done very quickly to meet very short timelines and we try to streamline every step.

5. We backed ourselves into a corner with the old MTA and now we are trying to get out. Please help.

Thanks,
Nancy

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Sent: Friday, January 09, 2009 5:41 PM
To: Knight, Janice (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

All,
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2. CDC's mission is to reduce influenza mortality and morbidity; the best way to do this is by global vaccination and ~90% the vaccine used worldwide is produced by pharmaceutical companies.

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4. For example, in 2006-2007 HHS gave $1 billion to 4 vaccine companies (no typos here, yes this is a done deal) to promote development of influenza vaccine manufacturing capacity in the continental USA.

5. To promote #2 and address #3, CDC makes the candidate vaccine strains and distributes them free of charge globally to encourage companies to develop and manufacture vaccines to immunize people.

6. CDC should not try to collect royalties for the seasonal or pandemic influenza vaccine candidates because we do not contribute intellectual property and also because it counters what HHS wanted to accomplish under #4 and #5.

7. CDC transfers the material to companies worldwide and informs the recipient that the material was produced using a proprietary technology and they are responsible for not violating the law with the use of the material. Doing otherwise would entail CDC taking on an IP enforcement role.

8. If vaccine companies can make money selling influenza vaccines, this may translate into more and better vaccines, which will help accomplish CDC's mission. Win-win situation. Vaccine companies may have to pay royalties to the owners of the IP (be it (b)(4) St Jude, etc), it is not for CDC to sort that out. Let US-DOJ or US-DOC deal with such IP issues.

9. The main concern for CDC should be to liability: we do not want to be liable for anything as a result of giving a vaccine candidate to a Company.

What risks would CDC face by distributing vaccine candidates under a rather liberal MTA? Would such risks outweigh the substantial benefits?

Thanks,
Ruben

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, January 09, 2009 3:40 PM
To: Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: FW: MTA

All,

I have reviewed the documents from Sanofi Pasteur attached to the email below and I have some thoughts. The edited draft of the CDC Letter Agreement seems to me to give Sanofi unlimited commercialization rights and would exclude CDC from receiving any royalty on CDC's IP in the RG Reassortants. Granted they have a license from AstraZeneca, but what does CDC do about licensure of these viruses? Are we going to provide these materials for commercial sale without any license agreement and no royalties of any sort? I reviewed the 2008 NIBSC agreement and I am not clear what Article 6.2 grants. Is NIBSC giving Sanofi all IP in modifications and all derivatives? Would this be granting rights is advance, which I thought CDC didn't do? Article 6.3 restricts use of the original materials from commercialization, but does not address IP that might remain within a modification or derivative.

Bottom line is under what terms does CDC allow commercialization of the RG Reassortants? I have attached blank templates of the Biological Materials License Agreement (BMLA) and my most current copy of the Proprietary Technology License Agreement (PTLA) for your information. In addition, in the BMLA we have used the following addition where provision by the commercial Licensee to developing countries was applicable:

"*d. An earned royalty that will be reduced to one half percent (0.5%) of* ***Net Sales*** *on* ***Licensed Products*** *sold in countries classified as low-income and lower-middle-income economies by the World Bank (www.worldbank.org). Classification will be reassessed at the beginning of each calendar year.* "

Janice

Janice C. Knight
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Wednesday, January 07, 2009 5:37 PM
To: Miller, Daniel S.(HHS/OGHA); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO)
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: FW: MTA

All,

It has been a few years since development of the terms of the MTA (or Simple Letter of Agreement) under which candidate vaccine strains prepared at CDC using reverse genetics technology have been distributed to vaccine manufacturers. As you know, the IP landscape of influenza reverse genetics has changed in the recent past (b)(4) as negotiated licenses with several vaccine companies to use this technology. I am receiving requests from these companies to revisit the terms of the MTA/SLA for future pandemic vaccine strains (and even retroactively). I am attaching a copy on one such request as an example. It is in the best interest of HHS to enable the proposed activities regarding pandemic vaccines: "internal research and development as well as in clinical trials, product development, licensure, donation and commercialization". Sanofi claims to have worked out MTA with our counterpart in the UK (NIBSC) that allows them to do all these things (see attached document).

HHS may not want to change anything, or perhaps some favorable conditions could be granted. In any case, re-evaluating the MTA/SLA and establishing consensus on the course of action would be important to be able to respond to the requests from companies. Please let me know how you would like to proceed; i.e. teleconference, face to face meeting, who else needs to be involved and so on.

Best regards,

Ruben

Ruben Donis, PhD
Chief, Molecular Virology and Vaccines Branch
Influenza Division, NCIRD, CCID
Centers for Disease Control and Prevention
1600 Clifton Road - Mail Stop G-16
Atlanta, GA 30333
Phone: (404) 639-4968
Fax: (404) 639-2350

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Wednesday, January 07, 2009 3:45 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: RE: MTA

Hi Ruben, Here is what we have come up with.

We received material from CDC under the form of Letter Agreement that you provided. On its face the agreement restricts our use of material to activities in furtherance of a specific contract with HHS. We want to amend the letter agreement(s), with retroactive effect, to allow us to engage in internal research and development as well as in clinical trials, product development, licensure, donation and commercialization. As you may know, (b)(4) (now AstraZeneca) consolidated all of the IP rights related to reverse genetics and plasmid rescue and offered these rights up as a license package. We took a non-exclusive license from (b)(4), and that is a matter of public record. You can google for the press release that (b)(4) made. (they subsequently signed up most, if not all, of the other players). Alternatively, I would invite you to contact Mr. Atul Saran, Esq., Sr. Director and Secretary of (b)(4) He will be happy to confirm that we took a license, and I'm sure he will be willing to facilitate the proposed agreement between CDC and sanofi pasteur, as the license from (b)(4) to Sanofi Pasteur is royalty-bearing. He can be reached at: (301) 398-4759. We could also provide you with redacted copies of our license agreements, if that would help.

According to the terms of our agreements with (b)(4) we can do whatever we want with material derived from RG/plasmid rescue, and can practice such methods ourselves, except that we can't make NS-1 modifications, can't work with the A/Ann Arbor backbone, and can't make live, attenuated flu. We don't have any intention of doing any of these things.

One of our attorneys here, Tim Howe, took your draft letter agreement and made some modifications. His draft is attached as mark-up. He plans next to prepare a draft amendment to the existing agreements as an alternative to this approach, but if this form of Letter Agreement is satisfactory to CDC it will work for us.

So, if we understand correctly, CDC simply wanted to be sure that any recipient of these materials would respect the IP rights of third parties. We are doing that, and can amply document that. Hopefully that means we can move ahead quickly now to secure the rights we need to continue in our efforts towards pandemic preparedness.

Thank you, as always, for your help in these matters.

Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,
Swiftwater, PA.18370
570-957-2513

From: Donis, Ruben O. (CDC/CCID/NCIRD) [mailto:rvd6@cdc.gov]
Sent: Friday, November 28, 2008 1:09 PM
To: Hjorth, Richard (sanofi pasteur)
Subject: RE: MTA

Richard,

Please see the below generic Simple Letter Agreement and let me know what changes would be desirable for Sanofi.
I just want to be sure I am on the same page when this is brought to the attention of HHS.
Thanks,
Ruben

Letter Agreement
In response to the request of COMPANY X, Inc. ("RECIPIENT") made to the Centers for Disease Control and Prevention ("PROVIDER') to be provided with the Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG6 Reference Strain ("MATERIAL") possessed by the PROVIDER" the PROVIDER asks that the RECIPIENT agee to the following before the RECIPIENT receives the MATERIAL:

The MATERIAL will be used in accordance with the following contract which RECIPIENT has been awarded by US Department of Health and Human Services: HHSOxxxx. The MATERI.AL will be used by the RECIPIENT for the purpose of the research, development and manufacture of influenza vaccines for US Department of Health and Human Services. Commercialization of the MATERIAL or vaccine derived from the MATERIAL may require commercialization licenses from extant patent holder(s) of the reverse genetics methodology andlor products obtained using reverse genetics methods.

With the exception of the distribution of the MATERIAL and vaccine derived from the MATERIAL (a) among the RECIPIENT's (or its affiliates') facilities and operations in xxxx(b) to the US Department of Health and Human Services,
which the PROVIDER hereby consents to, the MATERIAL will not be further distributed by the RECIPIENT without the PROVIDER's written consent. The RECIPIENT shall refer to the PROVIDER any request for the MATERIAL by any individual or company outside of the RECIPIENT and its affiliates.

Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. THE PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITIHER EXPRESSED OR IMPLIED. TIHERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Unless prohibited by law, the RECIPIENT assumes all liability for claims for damages.

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Wednesday, November 26, 2008 3:05 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: RE: MTA

Thanks for the quick follow up. Tim is excited about this. Here's a note from him: All my contact has been with Janice Knight in Tech Transfer. She's spoken with their OGC but I have not.

While I'm at it, in anticipation of a successful resolution of the dilemna and perhaps as a test case would you be willing to ship us your A/Chicken/India/NIV33407/2006? Also, the list we saw said the FDA had A/Duck/Laos/3295/2006. I didn't think FDA made these. Is this yours?

(b)(4)

Thanks again,
Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,
Swiftwater, PA.18370
570-957-2513

From: Donis, Ruben O. (CDC/CCID/NCIRD)
To: 'Richard.Hjorth@sanofipasteur.com'
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD)
Sent: Tue Nov 25 22:42:15 2008
Subject: FW: MTA

Hi Richard,
I see your point. I think we are moving towards CDC providing rg-derived vaccine candidates to manufacturers without any use restrictions – CDC will simply ask for waivers of liability and inform recipients that they are reponsible for compliance with IP laws.

I am copying Michael Shaw and Nancy Cox who have been in discussions about updating the MTA – not sure if the CDC legal folks are going to embrace this liberal approach.

Best regards,
Ruben

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Tuesday, November 25, 2008 10:11 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: FW: MTA

Hi Ruben,
I wonder if I can enlist your help with a mutually beneficial endeavor. One of our senior lawyers, Tim Howe, has been trying to work on this with some CDC lawyers and they don't seem to be getting very far. The issue is that you are making pre-pandemic vaccine viruses but right now, there are too many restrictions on their use in the CDC Simple Letter Agreements for them to be of much use to us. We would like to be able to use these strains to make commercial vaccines and to make donations to WHO. We've already commited as a company to donate to WHO.
We already have worked out an agreement with NIBSC [attached] that allows us to do all these things. Perhaps this could be a model for a similar CDC agreement.
I am hoping you might know the right people to speak with that may be able to move this along. I would hate to have to ask the NIBSC to make the same viruses you have already made just so we can use them. As you know, we already have an agreement with (b)(4) to use their reverse genetics so that should not be a concern.
Thanks for any help you can provide,
Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,
Swiftwater, PA.18370
570-957-2513

THIS MATERIALS TRANSFER AGREEMENT is made on 12 June 2008 (**"Effective Date"**)

BETWEEN

(1) **NATIONAL BIOLOGICAL STANDARDS BOARD** which manages the **NATIONAL INSTITUTE FOR BIOLOGICAL STANDARDS AND CONTROLS** whose office is at Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG (**"Provider"**); and

(2) **SANOFI PASTEUR SA**, a company existing and organised under the laws of the Republic of France, having its registered head office at 2 Avenue Pont Pasteur, 69007 Lyon, France and its affiliate Sanofi Pasteur Inc with offices at Discovery Drive, Swiftwater, PA 18370, United States of America (**"Recipient"**).

BACKGROUND:

The Provider has developed and owns (or is otherwise authorised to use) the Materials and Information which were developed with proprietary technology from the Mount Sinai School of Medicine (both as defined below).

The Recipient and the Principal Scientists wish to obtain the Materials and Information from the Provider solely for the purposes described herein.

The Provider agrees to provide the Materials and Information in accordance with the provisions set out below.

Under earlier agreements between the parties dated 26 March 2004 (in the name of Aventis Pasteur SA) and 12 May 2007 the Provider has previously provided Materials to the Recipient which the parties now wish to treat as if provided under this agreement.

In consideration of the mutual covenants and undertakings set out below **THE PARTIES AGREE** as follows:

1 Definitions

In this Agreement unless the context otherwise requires:

"Commencement Date" means the Effective Date;

"Field" means the use of the Materials by the Recipient for the manufacture of a vaccine in line with Schedule 2, and the use of the resulting vaccine in clinical trials and for other purposes in line with Schedule 2. The Field specifically excludes the following activities:

- making or use of vaccines comprised of or containing live influenza viruses
- modification of the NS-1 gene and/or protein
- incorporation into the vaccine of the Ann Arbor A or B Backbones or portions thereof

"Group Company" means any subsidiary or holding company of the company in question and any subsidiary of such holding company (in each case from time to time), (and the terms "**subsidiary**" and "**holding company**" shall have the meanings given to them by Sections 736 and 736A Companies Act 1985);

"Information" means any information, data and know-how relating to the Materials disclosed by the Provider to the Recipient under this Agreement;

"Intellectual Property Rights" means any patent, copyright, database right, moral right, design right, registered design, trade mark, service mark, domain name, know-how, utility model, unregistered design or, where relevant, any application for any such right, or other industrial or intellectual property right subsisting anywhere in the world;

"Materials" means influenza strains provided by the Provider to the Recipient under this Agreement or under earlier agreements between the parties dated 12 May 2007 and 26 March 2004 (in the name of Aventis Pasteur SA) as set out in the Schedule 1;

"Principal Scientists" means Dr Catherine Gerdil and Dr Richard Hjorth ,of Sanofi Pasteur SA and Sanofi Pasteur Inc respectively

"Recipient Scientists" means the Principal Scientists and any research assistants, co-workers or other workers who may use any of the Materials and/or the Information.

2 Delivery of the Materials

2.1 Upon execution of this Agreement the Provider agrees to supply the Materials and the Information to the Recipient. The Recipient warrants and represents that they are fit, experienced equipped and authorised to handle the Materials under their local

regulations.

2.2 The Provider will provide any regulatory consents or licences required by the United Kingdom export authorities for export of the Materials to the Recipient. At the discretion of the Provider, any costs involved may be recovered from the recipient.

2.3 The Recipient will provide any regulatory consents or licences required by the relevant import authorities.

3 Use of the Materials and Information and Record Keeping

3.1 The Materials and the Information will only be used in the Field.

3.2 The Materials will not be made available by the Recipient to any person other than the Principal Scientists or those who are under the direct supervision of the Principal Scientists and who have entered into a contract with the Recipient which vests all Intellectual Property Rights created by that person in the Recipient.

3.3 The Recipient and the Principal Scientists will procure that full records are kept as to the use the Materials and the quantities held by them. Such records will be made available to the Provider at the Provider's request.

4 Research Results

4.1 The Recipient and the Principal Scientists will inform the Provider of the results of the research using the Materials and/or the Information upon the request of the Provider.

5 Limitation of Liability, Indemnity and Warranty

5.1 The Recipient and the Principal Scientists understand and agree that the Materials and the Information are provided on an "as is" basis and as such without any warranty or representation of any kind (express or implied) including, without limitation, of satisfactory quality or fitness for a particular purpose or that the use or supply of the Materials or the Information will not infringe any Intellectual Property Rights or other rights of any third party. Specifically, the Provider does not warrant or represent that the Materials are free from infectious or harmful agents.

5.2 The Provider does not warrant or represent that Materials supplied with any stated

phenotype are representative of any particular disease or behavioural model or genotype.

5.3 The Provider will not be liable in any way for the use or storage, or any other act by or omission, by the Recipient or the Recipient Scientists in respect of any of the Material and/or the Information.

5.4 The Recipient agrees to indemnify and keep indemnified the Provider and their employees, directors, officers, agents and advisors against any loss, claim, damage, expenses (including professional advisors' fees) or liability of whatsoever kind or nature arising out of, or in connection with, the use, handling, storage, or any other act or omission in respect of any of the Materials and/or the Information by or on behalf of the Recipient and/or the Recipient Scientists.

6 Intellectual Property Rights

6.1 The Materials and the Information and the Intellectual Property Rights subsisting in them belonging to the Provider remain the property of the Provider.

6.2 Any Intellectual Property Rights arising out of the Recipient's and the Principal Scientists' use of the Materials and/or the Information in the Field will vest in the Recipient.

6.3 Notwithstanding any statement herein to the contrary and in accordance with the provisions of Clause 5.1, the Recipient acknowledges that no right or licence is being granted under this Agreement to the Recipient under any third party Intellectual Property Rights to commercialise (including, but not limited to, stockpiling of any vaccine derived from use of the Materials) or sell the Materials or use the Information for commercialisation purposes. To the extent that any such rights or licenses are required, the Recipient acknowledges that it is the Recipient's responsibility to obtain such rights or licences from (a) the Material owners and/or exclusive licensees and/or (b) the holders or exclusive licencees of patents and/or patent applications of the reverse genetics methodology and/or products obtained using reverse genetics methods and/or (c) any third parties that may have applicable rights in the Materials and/or Information.

7 Confidentiality and Confidentiality Measures

7.1 Subject to Clause 8 below, the Recipient and the Principal Scientists will keep and procure to keep secret and confidential all Information belonging to the Provider disclosed or obtained as a result of the relationship of the parties under this Agreement and will not use nor disclose the same save for the purposes of the proper performance of this Agreement or with the prior written consent of the Provider. Where disclosure is made to any employee, consultant, sub-contractor or agent, it shall be done subject to obligations equivalent to those set out in this Agreement and the Recipient and the Principal Scientists agree to ensure that if the Provider so requests prior to such disclosure such employee, consultant, sub-contractor or agent enters into a deed of covenant with the Provider in a form reasonably acceptable to the Provider containing obligations equivalent to those set out in this Clause 7. The Recipient and the Principal Scientists will procure that any such employee, consultant, sub-contractor or agent complies with such obligations. The Recipient and the Principal Scientists shall be responsible to the Provider in respect of any disclosure or use of such Information by a person to whom disclosure is made.

7.2 The obligations of confidentiality in this Clause 7 shall not extend to any matter which the Recipient or the Principal Scientists can show:

is in, or has become part of, the public domain other than as a result of a breach of the obligations of confidentiality under this Agreement; or

was independently disclosed to it by a third party entitled to disclose the same; or

is required to be disclosed under any applicable law, or by order of a court or governmental body or authority of competent jurisdiction.

7.3 The Recipient and the Principal Scientists will procure that the Materials, the Information (and any copies thereof) and any information generated by the Recipient Scientists will be kept separate.

8 Publication

8.1 The Recipient and the Recipient Scientists will have the right to publish research papers or publicly disclose information pertaining to or resulting from use of the

Materials and/or the Information.

9 Term and Termination

9.1 This Agreement will come into force on the Commencement Date and (subject to the provisions for earlier termination in Clause 9.2 below) will continue in force for ten years thereafter.

The Provider may immediately terminate this Agreement without payment of compensation or other damages caused to the Recipient solely by such termination by giving notice in writing to the Recipient or the Principal Scientist if any one or more of the following events happens:

(a) commits a material breach of any of its obligations under this Agreement which is incapable of remedy;

(b) the Recipient fails to remedy, where it is capable of remedy, or persists in any breach of any of its obligations under this Agreement after having been required in writing to remedy or desist from such breach within a period of 30 days;

(c) the Recipient proposes a voluntary arrangement within the meaning of Section 1 or Section 253 of the Insolvency Act 1986, or an interim order is made in relation to the other party under Section 252 of the Insolvency Act 1986, or any other steps are taken or negotiations commenced by the other party or any of its creditors with a view to proposing any kind of composition, compromise or arrangement involving the other party and any of its creditors;

(d) the Recipient has any distress or execution levied on its assets which is not paid out within seven days of it being levied;

(e) the Recipient is deemed to be unable to pay its debts within the meaning of Section 123 of the Insolvency Act 1986, or calls a meeting for the purpose of passing a resolution to wind it up, or such a resolution is passed or the other party presents, or has presented, a petition for a winding up order, or presents, or has presented, a petition to appoint an administrator, or has an administrative receiver, or receiver appointed over all or any part of its business, undertaking, property or assets;

(f) the Recipient stops or suspends making payments (whether of principal or interest) with respect to all or any class of its debts or announces an intention to do so or the other party suspends or ceases or threatens to suspend or cease to carry on its business;

(g) a secured lender to the Recipient takes any steps to obtain possession of the property on which it has security or otherwise to enforce its security;

(h) the Recipient suffers or undergoes any procedure analogous to any of those specified in Clause 9.2(e) to (g) inclusive above or any other procedure available in the country in which the other party is constituted, established or domiciled against or to an insolvent debtor or available to the creditors of such a debtor;

(i) the Provider has received written notice from the owners, holders, exclusive licencees and/or other third parties described in Clause 6.3 that the Recipient or the Principal Scientists do not have the rights necessary to use the Materials as contemplated by this Agreement.

9.2 Should the Recipient undergo a change of Control, or propose a voluntary agreement as defined in 9.2 (c), then they will inform the Provider of this fact within one month of the public announcement of the proposed change of Control. For the purposes of this Clause 9.3, "Control" has the meaning specified in Section 416 of the Income and Corporation Taxes Act 1988

9.3 The Provider may terminate this Agreement immediately by written notice to the Recipient, without payment of compensation or other damages caused to the Recipient solely by such termination, if the Recipient undergoes a change of Control (provided that such notice is given to the Recipient by the Provider within three months of the Provider becoming aware of such change of Control).

9.4 The termination of this Agreement shall be without prejudice to the rights and remedies of either party which may have accrued up to the date of termination.

10 Consequences of Termination or Expiry

10.1 Upon termination or expiry of this Agreement for any reason whatsoever:

(a) (subject to Clause 9.5 above) the relationship of the parties shall cease and the

rights or licences granted under or pursuant to this Agreement will cease to have effect save as (and to the extent) expressly provided for in this Clause 10;

(b) the provisions of any provision which expressly or by implication is intended to come into or remain in force on or after termination shall continue in full force and effect;

(c) each of the parties shall immediately return to the other parties (or, if the other parties so requests by notice in writing, destroy) all of the other parties' property in their possession at the date of termination, including all Confidential Information of the other parties together with all copies of such Confidential Information and shall certify that it has done so, and shall make no further use of such Confidential Information.

(d) the Recipient shall destroy all Information and materials and certify this action to the Provider or, at the request of the Provider, deliver up to the Provider all Information and Materials, including all copies of such Information and Materials thereof.

11 Assignment

11.1 This Agreement is personal to the Recipient. The Recipient will not assign, delegate, sub-contract, transfer, charge or otherwise dispose of all or any of its rights and responsibilities under this Agreement. If there are changes to the details of the Principal Scientists which materially affect their involvement in this agreement, the Provider must be informed immediately. Other individuals may then be substituted, subject to agreement with the Provider.

12 The Rights of Third Parties

12.1 Subject to Clause 12.2 below, the Contracts (Rights of Third Parties) Act 1999 shall not apply to this Agreement. No person who is not a party to this Agreement (including any employee, officer, agent, representative or subcontractor of either party) shall have the right (whether under the Contracts (Rights of Third Parties) Act 1999 or otherwise) to enforce any term of this Agreement which expressly or by implication confers a benefit on that person without the express prior agreement in writing of the parties which agreement must refer to this clause.

12.2 The Parties agree and accept that the provisions of Clause 6.3 above confer benefits on, and protect the Intellectual Property Rights belonging to, third parties with the right of enforcement.

13 General

13.1 The parties will not pledge the credit of the other parties nor represent themselves as being any one of the other parties nor an agent, partner, employee or representative of the other parties and the parties will not hold themselves out as such nor as having any power or authority to incur any obligation of any nature, express or implied, on behalf of the other parties and nothing in this Agreement will create, or be deemed to create, a partnership or joint venture or relationship of employer and employee or principal and agent between the parties and no employee of any party will be deemed to be or have become an employee of the other parties. Neither party may use the other party's name or trademarks in any public disclosure, without the named parties prior written consent.

13.2 This Agreement contains the entire agreement between the parties in relation to its subject-matter. Each of the parties irrevocably and unconditionally waives any right it may have to claim damages for, and/or to rescind this Agreement because of, breach of any warranty not contained in this Agreement, or any misrepresentation whether or not contained in this Agreement, unless such misrepresentation was made fraudulently.

13.3 No purported alteration or variation of this Agreement shall be effective unless it is in writing, refers specifically to this Agreement and is signed by each of the parties to this Agreement.

13.4 The rights and remedies of any party in respect of this Agreement will not be diminished, waived or extinguished by the granting of any indulgence, forbearance or extension of time granted by such party to the others nor by any failure of, or delay by the said party in ascertaining or exercising any such rights or remedies. Any waiver of any breach of this Agreement shall be in writing. The waiver by any party of any breach of this Agreement will not prevent the subsequent enforcement of that provision and will not be deemed to be a waiver of any subsequent breach of that or any other provision.

13.5 If at any time any part of this Agreement (including any one or more of the clauses of this Agreement or any sub-clause or paragraph or any part of one or more of these clauses) is held to be or becomes void or otherwise unenforceable for any reason under any applicable law, the same shall be deemed omitted from this Agreement and the validity and/or enforceability of the remaining provisions of this Agreement shall not in any way be affected or impaired as a result of that omission.

13.6 This Agreement may be entered into in the form of two or more counterparts, each executed by one or more of the parties but, taken together, executed by all, and, provided that all the parties shall so enter into the Agreement, each of the executed counterparts, when duly exchanged or delivered, will be deemed to be an original but, taken together, they shall constitute one instrument.

14 Law

14.1 This Agreement and any dispute or claim arising out of or in connection with it shall be governed by, and construed in accordance with, the laws of England.

15 Jurisdiction

15.1 All disputes or claims arising out of or relating to this Agreement shall be subject to the non-exclusive jurisdiction of the English Courts to which the parties irrevocably submit.

IN WITNESS OF THE ABOVE the parties have signed this Agreement on the date written at the head of this Agreement.

SIGNED by Victor Knight (Board Secretary)

.....
(Authorised Signatory)

on behalf of
NATIONAL BIOLOGICAL STANDARDS BOARD

SIGNED by

.....
(Authorised Signatory)

on behalf of

RECIPIENT

ACKNOWLEDGED by:

C. GEROR
(Principal Scientist)

R. HEATH
(Principal Scientist)

Schedule 1

The Materials

1. Material provided to the Recipient under the earlier agreement between the parties dated 12 May 2007:

   NIBRG-23 - an A/Turkey/Turkey/1/2005/(H5N1) Vaccine Reference Strain Generated by Reverse Genetics

2. Material provided to the Recipient under the earlier agreement between the parties (in the name of Aventis Pasteur SA) dated 26 March 2004:

   NIBRG-14 - an A/Viet Nam/1194/1/2004 (H5N1) Vaccine Reference Strain Generated by Reverse Genetics.

Schedule 2

The Materials may be used for some or all of the activities listed below within the constraints imposed by any third party as indicated in Clauses 6.3 and 12.2:

- Production of seed stocks from growth in embryonated hens' eggs or on mammalian cells.

- Production and commercialization of inactivated influenza vaccine.

- Evaluation of virus yield following growth of the Materials in embryonated hens' eggs or on mammalian cells.

- Tests of antigenic properties of the Materials using reference sera.

- Infection or vaccination of animals with the Materials in order to produce reference antibody preparations.

- Sequencing of the Materials' gene segments.

- Production of pilot lots of inactivated vaccine from the Materials for quality control evaluation, for vaccination and efficacy studies in small animals, or for clinical trial studies in humans. As a challenge virus in vaccine efficacy studies.

- Production of virus antigen from the Materials for use in diagnostic kits. The kits will not be used for commercial or revenue-generating purposes.

- Assessment of viral inactivation and/or removal procedures for public health purposes.

Schedule 3

Delivery

NIBSC

THIS MATERIALS TRANSFER AGREEMENT is made on May 12, 2007

BETWEEN

(1) **NATIONAL BIOLOGICAL STANDARDS BOARD** which manages the **NATIONAL INSTITUTE FOR BIOLOGICAL STANDARDS AND CONTROLS** whose office is at Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG ("**Provider**"); and

(2) **Sanofi Pasteur S.A.,** formerly Aventis Pasteur S.A, a company existing and organised under the laws of the Republic of France, having its registered head office at 2, avenue Pont Pasteur, 69007, Lyon, France and its affiliate Sanofi Pasteur, Inc., with offices at Discovery Drive, Swiftwater, PA 18370, (hereinafter, individually or collectively, "Recipient"); and

(3) Catherine Gerdil and Richard Hjorth (**"Principal Scientist"** (Sanofi Pasteur S.A. and Sanofi Pasteur, Inc., respectively)).

BACKGROUND:

The Provider has developed and owns (or is otherwise authorised to use) the Materials and Information which were developed with proprietary technology (both as defined below).

The Recipient and the Principal Scientist(s) wish to obtain the Materials and Information from the Provider solely for the purposes described herein.

The Provider agrees to provide the Materials and Information in accordance with the provisions set out below.

In consideration of the mutual covenants and undertakings set out below **THE PARTIES AGREE** as follows:

1 **Definitions**

In this Agreement unless the context otherwise requires:

"Commencement Date" means the Effective Date;

"Field" means the use of the Materials by the Recipient for the manufacture of a vaccine from the direct progeny of an influenza strain (NIBRG-23, see Schedule 1) as further described in Schedule 2, and the use of the resulting vaccine for research and development activities, in clinical trials, to immunize critical workforce personnel and for use in preparing and delivering stockpiles in response to government tenders, provided always that such use does not infringe the Intellectual Property Rights or any other rights of the owners of the plasmids on which the Materials are based. The Field specifically excludes the use of the Materials to generate modified derivatives or modifications of the Materials. Recipient shall be allowed to manufacture vaccine from the direct progeny of the provided influenza strain. For the avoidance of doubt, the Field does not include the use of the Materials to create a reassortment virus (by natural or artificial means).

"Group Company" means any subsidiary or holding company of the company in question and any subsidiary of such holding company (in each case from time to time), (and the terms **"subsidiary"** and **"holding company"** shall have the meanings given to them by Sections 736 and 736A Companies Act 1985);

"Information" means any information, data and know-how relating to the Materials disclosed by the Provider to the Recipient under this Agreement;

"Intellectual Property Rights" means any patent, copyright, database right, moral right, design right, registered design, trade mark, service mark, domain name, know-how, utility model, unregistered design or, where relevant, any application for any such right, or other industrial or intellectual property right subsisting anywhere in the world;

"Materials" means influenza strain A/Turkey/Turkey/1/2005 NIBRG-23 provided by the Provider to the Recipient under this Agreement, as set out in the Schedule 1;

"Recipient Scientists" means the Principal Scientist and any research assistants, co-workers or other workers who may use any of the Materials and/or the Information.

2 Delivery of the Materials

2.1 Upon execution of this Agreement the Provider agrees to supply the Materials and the Information to the Recipient. The Recipient warrants and represents that they are fit, experienced equipped and authorised to handle the Materials under their local regulations.

2.2 The Provider will provide any regulatory consents or licences required by the United Kingdom export authorities for export of the Materials to the Recipient. At the discretion of the Provider, any costs involved may be recovered from the recipient.

2.3 The Recipient will provide any regulatory consents or licences required by the relevant import authorities.

3 Use of the Materials and Information and Record Keeping

3.1 The Materials and the Information will only be used in the Field for manufacture and use of a vaccine, including conducting clinical trials and preparing stockpiles of the produced vaccine for delivery to governmental agencies. Recipient agrees not to make modified derivatives or modifications of the Materials, but Recipient shall be allowed to manufacture vaccine from the direct progeny of the provided influenza strain. For the avoidance of doubt, the Field does not include the use of the Materials to create a reassortment virus (by natural or artificial means). Recipient will destroy any naturally created reassortment viruses which Recipient becomes aware of and which may inadvertently arise during the use of the Materials to create direct progeny of the provided strain.

3.2 The Materials will not be made available by the Recipient or the Principal Scientist(s) to any person other than those who are under the direct supervision of the Principal Scientist(s) and who have entered into a contract with the Recipient which vests all Intellectual Property Rights created by that person in the Recipient.

3.3 The Recipient and the Principal Scientist(s) will procure that full records are kept as to the use the Materials and the quantities held by them. Such records will be made available to the Provider at the Provider's request and at the end of the term of this Agreement.

4 Research Results

4.1 The Recipient and the Principal Scientist(s) will inform the Provider of the results of the research using the Materials and/or the Information upon the request of the Provider.

5 Limitation of Liability, Indemnity and Warranty

5.1 The Recipient and the Principal Scientist(s) understand and agree that the Materials and the Information are provided on an "as is" basis and as such without any warranty or representation of any kind (express or implied) including, without limitation, of satisfactory quality or fitness for a particular purpose or that the use or supply of the Materials or the Information will not infringe any Intellectual Property Rights or other rights of any third party. Specifically, the Provider does not warrant or represent that the Materials are free from infectious or harmful agents.

5.2 The Provider does not warrant or represent that Materials supplied with any stated phenotype are representative of any particular disease or behavioural model or genotype.

5.3 The Provider will not be liable in any way for the use or storage, or any other act by or omission, by the Recipient or the Recipient Scientist(s) in respect of any of the Material and/or the Information.

5.4 The Recipient agrees to indemnify and keep indemnified the Provider and their employees, directors, officers, agents and advisors against any loss, claim, damage, expenses (including professional advisors' fees) or liability of whatsoever kind or nature arising out of, or in connection with, the use, handling, storage, or any other act or omission in respect of any of the Materials and/or the Information by or on behalf of the Recipient and/or the Recipient Scientist(s).

6 Intellectual Property Rights

6.1 The Materials and the Information and the Intellectual Property Rights subsisting in them remain the property of the Provider.

6.2 Any Intellectual Property Rights arising out of the Recipient's and the Principal Scientist's use of the Materials and/or the Information in the Field will vest in the Recipient.

7 Confidentiality and Confidentiality Measures

7.1 Subject to Clause 8 below, the Recipient and the Principal Scientist(s) will keep and

procure to be keep secret and confidential all Information belonging to the Provider disclosed or obtained as a result of the relationship of the parties under this Agreement and will not use nor disclose the same save for the purposes of the proper performance of this Agreement or with the prior written consent of the Provider. Where disclosure is made to any employee, consultant, sub-contractor or agent, it shall be done subject to obligations equivalent to those set out in this Agreement and the Recipient and the Principal Scientist(s) agree to ensure that if the Provider so requests prior to such disclosure such employee, consultant, sub-contractor or agent enters into a deed of covenant with the Provider in a form reasonably acceptable to the Provider containing obligations equivalent to those set out in this Clause 7. The Recipient and the Principal Scientist(s) will procure that any such employee, consultant, sub-contractor or agent complies with such obligations. The Recipient and the Principal Scientist shall be responsible to the Provider in respect of any disclosure or use of such Information by a person to whom disclosure is made.

7.2 The obligations of confidentiality in this Clause 7 shall not extend to any matter which the Recipient or the Principal Scientist(s) can show:

is in, or has become part of, the public domain other than as a result of a breach of the obligations of confidentiality under this Agreement; or

was independently disclosed to it by a third party entitled to disclose the same; or

is required to be disclosed under any applicable law, or by order of a court or governmental body or authority of competent jurisdiction.

7.3 The Recipient and the Principal Scientist(s) will procure that the Materials, the Information (and any copies thereof) and any information generated by the Recipient Scientist(s) will be kept separate.

8 Publication

8.1 The Recipient shall be allowed to publish research papers or publicly disclose information pertaining to or resulting from use of the Materials and/or the Information report after prior review by NIBSC. The Recipient shall submit the proposed disclosure or publication for review to NIBSC at least forty-five (45) days prior to the proposed disclosure or publication date, and NIBSC will respond within thirty (30)

days after submission. NIBSC may not unreasonably withhold their written consent of its publication

9 Term and Termination

9.1 This Agreement will come into force on the Commencement Date and (subject to the provisions for earlier termination in Clause 9.2 below) will continue in force thereafter unless and until either party gives to the other party not less than 3 months' prior written notice of termination.

9.2 The Provider may immediately terminate this Agreement without payment of compensation or other damages caused to the Recipient or the Principal Scientist(s) solely by such termination by giving notice in writing to the Recipient or the Principal Scientist(s) if any one or more of the following events happens:

(a) the Recipient or the Principal Scientist(s) commits a material breach of any of its obligations under this Agreement which is incapable of remedy;

(b) the Recipient or the Principal Scientist(s) fails to remedy, where it is capable of remedy, or persists in any breach of any of its obligations under this Agreement after having been required in writing to remedy or desist from such breach within a period of 30 days;

(c) the Recipient proposes a voluntary arrangement within the meaning of Section 1 or Section 253 of the Insolvency Act 1986, or an interim order is made in relation to the other party under Section 252 of the Insolvency Act 1986, or any other steps are taken or negotiations commenced by the other party or any of its creditors with a view to proposing any kind of composition, compromise or arrangement involving the other party and any of its creditors;

(d) the Recipient has any distress or execution levied on its assets which is not paid out within seven days of it being levied;

(e) the Recipient is deemed to be unable to pay its debts within the meaning of Section 123 of the Insolvency Act 1986, or calls a meeting for the purpose of passing a resolution to wind it up, or such a resolution is passed or the other party presents, or has presented, a petition for a winding up order, or presents, or has presented, a

petition to appoint an administrator, or has an administrative receiver, or receiver appointed over all or any part of its business, undertaking, property or assets;

(f) the Recipient stops or suspends making payments (whether of principal or interest) with respect to all or any class of its debts or announces an intention to do so or the other party suspends or ceases or threatens to suspend or cease to carry on its business;

(g) a secured lender to the Recipient takes any steps to obtain possession of the property on which it has security or otherwise to enforce its security;

(h) the Recipient suffers or undergoes any procedure analogous to any of those specified in Clause 9.2(e) to (g) inclusive above or any other procedure available in the country in which the other party is constituted, established or domiciled against or to an insolvent debtor or available to the creditors of such a debtor.

9.3 Should the Recipient undergo a change of Control, or propose a voluntary agreement as defined in 9.2 (c), then they will inform the Provider of this fact within one month of the public announcement of the proposed change of Control. For the purposes of this Clause 9.3, "Control" has the meaning specified in Section 416 of the Income and Corporation Taxes Act 1988

9.4 The Provider may terminate this Agreement immediately by written notice to the Recipient, without payment of compensation or other damages caused to the Recipient solely by such termination, if the Recipient undergoes a change of Control (provided that such notice is given to the Recipient by the Provider within three months of the Provider becoming aware of such change of Control).

9.5 The termination of this Agreement shall be without prejudice to the rights and remedies of either party which may have accrued up to the date of termination.

10 Consequences of Termination or Expiry

10.1 Upon termination or expiry of this Agreement for any reason whatsoever:

(a) (subject to Clause 9.5 above) the relationship of the parties shall cease and the rights or licences granted under or pursuant to this Agreement will cease to have effect

save as (and to the extent) expressly provided for in this Clause 10;

(b) the provisions of any provision which expressly or by implication is intended to come into or remain in force on or after termination shall continue in full force and effect;

(c) each of the parties shall immediately return to the other parties (or, if the other parties so requests by notice in writing, destroy) all of the other parties' property in their possession at the date of termination, including all Confidential Information of the other parties together with all copies of such Confidential Information and shall certify that it has done so, and shall make no further use of such Confidential Information.

(d) the Recipient shall deliver up to the Provider all Information and Materials, including all copies of such Information and Materials thereof, except that Recipient may keep one copy of such Information within its legal files solely for archival purposes.

11 Assignment

11.1 This Agreement is personal to the Recipient and the Principal Scientist(s). The Recipient and Principal Scientist(s) will not assign, delegate, sub-contract, transfer, charge or otherwise dispose of all or any of its or their rights and responsibilities under this Agreement. If there are changes to the details of the Principal Scientist(s) which materially affect their involvement in this agreement, the Provider must be informed immediately. Another individual may then be substituted, subject to agreement with the Provider.

12 The Rights of Third Parties

12.1 The Contracts (Rights of Third Parties) Act 1999 shall not apply to this Agreement. No person who is not a party to this Agreement (including any employee, officer, agent, representative or subcontractor of either party) shall have the right (whether under the Contracts (Rights of Third Parties) Act 1999 or otherwise) to enforce any term of this Agreement which expressly or by implication confers a benefit on that person without the express prior agreement in writing of the parties which agreement must refer to this clause.

13 General

13.1 The parties will not pledge the credit of the other parties nor represent themselves as being any one of the other parties nor an agent, partner, employee or representative of the other parties and the parties will not hold themselves out as such nor as having any power or authority to incur any obligation of any nature, express or implied, on behalf of the other parties and nothing in this Agreement will create, or be deemed to create, a partnership or joint venture or relationship of employer and employee or principal and agent between the parties and no employee of any party will be deemed to be or have become an employee of the other parties. Neither party may use the other party's name or trademarks in any public disclosure, without the named parties prior written consent.

13.2 This Agreement contains the entire agreement between the parties in relation to its subject-matter. Each of the parties irrevocably and unconditionally waives any right it may have to claim damages for, and/or to rescind this Agreement because of, breach of any warranty not contained in this Agreement, or any misrepresentation whether or not contained in this Agreement, unless such misrepresentation was made fraudulently.

13.3 No purported alteration or variation of this Agreement shall be effective unless it is in writing, refers specifically to this Agreement and is signed by each of the parties to this Agreement.

13.4 The rights and remedies of any party in respect of this Agreement will not be diminished, waived or extinguished by the granting of any indulgence, forbearance or extension of time granted by such party to the others nor by any failure of, or delay by the said party in ascertaining or exercising any such rights or remedies. Any waiver of any breach of this Agreement shall be in writing. The waiver by any party of any breach of this Agreement will not prevent the subsequent enforcement of that provision and will not be deemed to be a waiver of any subsequent breach of that or any other provision.

13.5 If at any time any part of this Agreement (including any one or more of the clauses of this Agreement or any sub-clause or paragraph or any part of one or more of these clauses) is held to be or becomes void or otherwise unenforceable for any reason

under any applicable law, the same shall be deemed omitted from this Agreement and the validity and/or enforceability of the remaining provisions of this Agreement shall not in any way be affected or impaired as a result of that omission.

13.6 This Agreement may be entered into in the form of two or more counterparts, each executed by one or more of the parties but, taken together, executed by all, and, provided that all the parties shall so enter into the Agreement, each of the executed counterparts, when duly exchanged or delivered, will be deemed to be an original but, taken together, they shall constitute one instrument.

14 Law

14.1 This Agreement and any dispute or claim arising out of or in connection with it shall be governed by, and construed in accordance with, the laws of England.

15 Jurisdiction

15.1 All disputes or claims arising out of or relating to this Agreement shall be subject to the non-exclusive jurisdiction of the English Courts to which the parties irrevocably submit.

IN WITNESS OF THE ABOVE the parties have signed this Agreement on the date written at the head of this Agreement.

SIGNED by Victor Knight (Board Secretary)

.....
(Authorised Signatory)

on behalf of
NATIONAL BIOLOGICAL STANDARDS BOARD

SIGNED by Michel DeWilde
SVP RED
on behalf of
SANOFI PASTEUR SA and its Affiliate, SANOFI PASTEUR, INC.

.....
(Authorised Signatory)

June 4, 2007

SIGNED by Catherine Gerdil

.....
(Principal Scientist, Sanofi Pasteur S.A)

July 11, 2007

SIGNED by Richard Hjorth

.....
26 July 2007
(Principal Scientist, Sanofi Pasteur, Inc.)

Schedule 1

The Materials

NIBRG-23 - an A/Turkey/Turkey/1/2005// (H5N1) Vaccine Reference Strain Generated by Reverse Genetics

Schedule 2

Details of testing

NIBRG-23 virus may be used for some or all of the activities listed below:

- Production of seed stocks from growth in embryonated hens' eggs or on mammalian cells.
- Evaluation of virus yield following growth of NIBRG-14 in embryonated hens' eggs or on mammalian cells.
- Tests of antigenic properties of NIBRG-23 using reference sera.
- Infection of ferrets with NIBRG-23 in order to produce reference post infection sera.
- Sequencing of NIBRG-23 influenza virus gene segments.
- Production of pilot lots of inactivated NIBRG-23 vaccine for quality control evaluation, for vaccination and challenge studies in small animals, or for clinical trial studies in humans. These studies will be for research purposes only.
- Production of commercial lots of inactivated NIBRG-23 vaccine for use in further development activities, e.g., to determine scalability of manufacturing processes, for ongoing clinical trials, for immunization of critical workforce and for preparation of stockpiles for use in the event of a pre-pandemic or pandemic emergency. Such activities shall not infringe the Intellectual Property Rights or any other rights of either the owners of the plasmids on which the Materials are based or the owners of the reverse genetic engineering processes used to make these strains safe.

Schedule 3

Delivery

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Letter Agreement

In response to the request of Sanofi Pasteur Inc., together with its affiliate Sanofi Pasteur S.A.~~COMPANY X, Inc.~~ ("RECIPIENT") made to the Centers for Disease Control and Prevention ("PROVIDER") to be provided with the Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG6 Reference Strain ("MATERIAL") possessed by the PROVIDER" the PROVIDER asks that the RECIPIENT agree to the following before the RECIPIENT receives the MATERIAL:

The MATERIAL will be used in accordance with the terms of the following contract which RECIPIENT has been awarded by US Department of Health and Human Services: HHSOxxxx. The MATERIAL will be used by the RECIPIENT for the purpose of the research, development and manufacture of influenza vaccines for US Department of Health and Human Services as well as for other purposes, including but not limited to internal research and development activities, immunization of our critical work force and for donation and sale to parties in addition to HHS.

The parties hereto acknowledge that cCommercialization of the MATERIAL or vaccine derived from the MATERIAL may require commercialization licenses from extant patent holder(s) of the reverse genetics methodology and/or products obtained using reverse genetics methods. RECIPIENT represents and warrants to PROVIDER that it has obtained the necessary commercialization licenses to reverse genetics methodology and, accordingly, has the right to conduct internal research and development activities and to produce vaccine derived from MATERIAL for any and all purposes, including commercial purposes, but solely to the extent that use of the MATERIAL does not infringe the intellectual property rights of third parties. For the avoidance of doubt, for purposes of this Letter Agreement, MATERIAL shall include progeny and unmodified derivatives of MATERIAL, but shall not include modified derivatives or inactivated viral vaccines produced using such MATERIAL. Any such modified derivatives and/or inactivated viral vaccines shall be and remain the property of the RECIPIENT.

With the exception of the distribution of the MATERIAL ~~and vaccine derived from the MATERIAL~~ (a) among the RECIPIENT's (or its affiliates') facilities and operations in Swiftwater, PA USA and Marcy l'Etoile, France ~~xxxx(b)~~ and~~to~~ the US Department of Health and Human Services, which the PROVIDER hereby consents to, the MATERIAL *per se* will not be further distributed by the RECIPIENT without the PROVIDER's written consent. The RECIPIENT shall refer to the PROVIDER any request for the MATERIAL by any individual or company outside of the RECIPIENT and its affiliates.

Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. THE PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Unless prohibited by law, the RECIPIENT assumes all liability for claims for damages.

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Cox, Nancy (CDC/CCID/NCIRD)
Sent: Sunday, January 11, 2009 2:48 PM
To: Watkins, Andrew (CDC/OD/OCSO); Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Berkley, Dale (NIH/OD) [E]
Cc: Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

Thanks to all for keeping up with this difficult issue and working toward a globally acceptable solution. This has not been easy!
Nancy

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Sunday, January 11, 2009 1:02 PM
To: Cox, Nancy (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Berkley, Dale (NIH/OD) [E]
Cc: Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

Folks,

I am in agreement with Ruben and Nancy's sentiments. During the course of our many discussions about influenza vaccine virus transfers, I believe we concluded that as long as the current system of transferring our standard vaccine virus candidates to vaccine manufacturers is successful, and neither requires nor would benefit substantially from the use of our formal technology transfer tools, then we should continue the approach that has worked for several decades. This, especially in light of the international concerns over use of influenza viruses obtained originally from sensitive countries, unless by licensing the viruses we can better ensure equitable distribution to those counties. Is that a role we wish to take on here?

At the same time, we must also make certain that we are not violating anyone else's legitimate rights or any obligations we have made to others. I believe we are past that point with (b)(4) (b)(4) at this point, provided we ensure that we make those rights clear to companies or other entities to which we transfer the viruses, as Janice has noted quite well.

In my opinion, and consistent with our many discussions, we should find a way to remove the restrictions on use of the reassortants, while ensuring we are clear about any restrictions that may be imposed by others, but we should get out of the middle of those rights as best we can.

I will need to see Tim Howe's markup of our Letter Agreement - it did not come through with this email chain. Ruben, Janice, can one of you please forward that to me?

Thanks,
Andrew

Andrew Watkins
Director, CDC Technology Transfer Office

From: Cox, Nancy (CDC/CCID/NCIRD)
Sent: Saturday, January 10, 2009 4:29 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Berkley, Dale (NIH/OD) [E]
Cc: Shaw, Michael (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

Janice,

More food for thought.

1. We have had many, many discussions about these matters leading up to the Intergovernmental Meeting held last December. NIH lawyer Dale Berkeley is very much aligned with us in our approach and I have copied him here.

2. We have **never** received royalties for any of the influenza viruses provided to vaccine manufacturers for vaccine manufacture during my entire tenure at CDC which is just over 33 years. If I am wrong someone please correct me.

3. Influenza B viruses used in influenza vaccines are almost always wild-type viruses and we provide them free of charge throughout the WHO system and to vaccine manufacturers on an annual basis, no strings attached.

4. Seasonal influenza A viruses provided to vaccine manufacturers are typically high growth reassortants that are produced by specialized laboratories but no royalties go to the country of origin, to the WHO or the experts that make the vaccine strain selection and provide the viruses to the specialized labs to make the high growth reassortants, nor to the specialized labs that make the seasonal high growth reassortants. The work has to be done very quickly to meet very short timelines and we try to streamline every step.

5. We backed ourselves into a corner with the old MTA and now we are trying to get out. Please help.

Thanks,
Nancy

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Friday, January 09, 2009 5:41 PM
To: Knight, Janice (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: MTA

All,
If I may, I will wear my intergalactic observer hat for a moment and make some comments:

1. CDC has access to many of the influenza viruses used in the derivation of reassortants by reverse genetics through its role as WHO Collaborating Center; therefore CDC is not the sole "owner" of said reassortants.

2. CDC's mission is to reduce influenza mortality and morbidity; the best way to do this is by global vaccination and ~90% the vaccine used worldwide is produced by pharmaceutical companies.

3. Vaccine manufacturing is a high risk business proposition: most big pharmas are very cautious about investing in vaccine product development (it may get worse before it gets better).

4. For example, in 2006-2007 HHS gave $1 billion to 4 vaccine companies (no typos here, yes this is a done deal) to promote development of influenza vaccine manufacturing capacity in the continental USA.

5. To promote #2 and address #3, CDC makes the candidate vaccine strains and distributes them free of charge globally to encourage companies to develop and manufacture vaccines to immunize people.

6. CDC should not try to collect royalties for the seasonal or pandemic influenza vaccine candidates because we do not contribute intellectual property and also because it counters what HHS wanted to accomplish under #4 and #5.

7. CDC transfers the material to companies worldwide and informs the recipient that the material was produced using a proprietary technology and they are responsible for not violating the law with the use of the material. Doing otherwise would entail CDC taking on an IP enforcement role.

8. If vaccine companies can make money selling influenza vaccines, this may translate into more and better vaccines, which will help accomplish CDC's mission. Win-win situation. Vaccine companies may have to pay royalties to the owners of the IP (be it (b)(4) St Jude, etc), it is not for CDC to sort that out. Let US-DOJ or US-DOC deal with such IP issues.

9. The main concern for CDC should be to liability: we do not want to be liable for anything as a result of giving a vaccine candidate to a Company.

What risks would CDC face by distributing vaccine candidates under a rather liberal MTA? Would such risks outweigh the substantial benefits?

Thanks,
Ruben

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, January 09, 2009 3:40 PM
To: Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD); Miller, Daniel S. (CDC/COGH/DGPPC); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: FW: MTA

All,

I have reviewed the documents from Sanofi Pasteur attached to the email below and I have some thoughts. The edited draft of the CDC Letter Agreement seems to me to give Sanofi unlimited commercialization rights and would exclude CDC from receiving any royalty on CDC's IP in the RG Reassortants. Granted they have a license from AstraZeneca, but what does CDC do about licensure of these viruses? Are we going to provide these materials for commercial sale without any licehse agreement and no royalties of any sort? I reviewed the 2008 NIBSC agreement and I am not clear what Article 6.2 grants. Is NIBSC giving Sanofi all IP in modifications and all derivatives? Would this be granting rights is advance, which I thought CDC didn't do? Article 6.3 restricts use of the original materials from commercialization, but does not address IP that might remain within a modification or derivative.

Bottom line is under what terms does CDC allow commercialization of the RG Reassortants? I have attached blank templates of the Biological Materials License Agreement (BMLA) and my most current copy of the Proprietary Technology License Agreement (PTLA) for your information. In addition, in the BMLA we have used the following addition where provision by the commercial Licensee to developing countries was applicable:

" *d. An earned royalty that will be reduced to one half percent (0.5%) of* ***Net Sales*** *on* ***Licensed Products*** *sold in countries classified as low-income and lower-middle-income economies by the World Bank (www.worldbank.org). Classification will be reassessed at the beginning of each calendar year.* "

Janice

Janice C. Knight

Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE

Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Wednesday, January 07, 2009 5:37 PM
To: Miller, Daniel S.(HHS/OGHA); Shapiro, Craig (HHS/OGHA); Blake-DiSpigna, Lisa (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO)
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: FW: MTA

All,

It has been a few years since development of the terms of the MTA (or Simple Letter of Agreement) under which candidate vaccine strains prepared at CDC using reverse genetics technology have been distributed to vaccine manufacturers. As you know, the IP landscape of influenza reverse genetics has changed in the recent past: (b)(4) has negotiated licenses with several vaccine companies to use this technology. I am receiving requests from these companies to revisit the terms of the MTA/SLA for future pandemic vaccine strains (and even retroactively). I am attaching a copy on one such request as an example. It is in the best interest of HHS to enable the proposed activities regarding pandemic vaccines: "internal research and development as well as in clinical trials, product development, licensure, donation and commercialization". Sanofi claims to have worked out MTA with our counterpart in the UK (NIBSC) that allows them to do all these things (see attached document).

HHS may not want to change anything, or perhaps some favorable conditions could be granted. In any case, re-evaluating the MTA/SLA and establishing consensus on the course of action would be important to be able to respond to the requests from companies. Please let me know how you would like to proceed; i.e. teleconference, face to face meeting, who else needs to be involved and so on.

Best regards,

Ruben

Ruben Donis, PhD
Chief, Molecular Virology and Vaccines Branch
Influenza Division, NCIRD, CCID
Centers for Disease Control and Prevention
1600 Clifton Road - Mail Stop G-16
Atlanta, GA 30333
Phone: (404) 639-4968
Fax: (404) 639-2350

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Wednesday, January 07, 2009 3:45 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: RE: MTA

Hi Ruben, Here is what we have come up with.

We received material from CDC under the form of Letter Agreement that you provided. On its face the agreement restricts our use of material to activities in furtherance of a specific contract with HHS. We want to amend the letter agreement(s), with retroactive effect, to allow us to engage in internal research and development as well as in clinical trials, product development, licensure, donation and commercialization. As you may know, MedImmune (now AstraZeneca) consolidated all of the IP rights related to reverse genetics and plasmid rescue and offered these rights up as a license package. We took a non-exclusive license from (b)(4) nd that is a matter of public record. You can google for the press release that (b)(4) made. (they subsequently signed up most, if not all, of the other players). Alternatively, I would invite you to contact Mr. Atul Saran, Esq., Sr. Director and Secretary of (b)(4) He will be happy to confirm that we took a license, and I'm sure he will be willing to facilitate the proposed agreement between CDC and sanofi pasteur, as the license from (b)(4) to Sanofi Pasteur is royalty-bearing. He can be reached at: (301) 398-4759. We could also provide you with redacted copies of our license agreements, if that would help.

According to the terms of our agreements with (b)(4) we can do whatever we want with material derived from RG/plasmid rescue, and can practice such methods ourselves, except that we can't make NS-1 modifications, can't work with the A/Ann Arbor backbone, and can't make live, attenuated flu. We don't have any intention of doing any of these things.

One of our attorneys here, Tim Howe, took your draft letter agreement and made some modifications. His draft is attached as mark-up. He plans next to prepare a draft amendment to the existing agreements as an alternative to this approach, but if this form of Letter Agreement is satisfactory to CDC it will work for us.

So, if we understand correctly, CDC simply wanted to be sure that any recipient of these materials would respect the IP rights of third parties. We are doing that, and can amply document that. Hopefully that means we can move ahead quickly now to secure the rights we need to continue in our efforts towards pandemic preparedness.

Thank you, as always, for your help in these matters.

Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,
Swiftwater, PA.18370
570-957-2513

From: Donis, Ruben O. (CDC/CCID/NCIRD) [mailto:rvd6@cdc.gov]
Sent: Friday, November 28, 2008 1:09 PM
To: Hjorth, Richard (sanofi pasteur)
Subject: RE: MTA

Richard,
Please see the below generic Simple Letter Agreement and let me know what changes would be desirable for Sanofi.
I just want to be sure I am on the same page when this is brought to the attention of HHS.
Thanks,
Ruben

Letter Agreement
In response to the request of COMPANY X, Inc. ("RECIPIENT") made to the
Centers for Disease Control and Prevention ("PROVIDER") to be provided with the Influenza A virus

reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG6 Reference Strain ("MATERIAL") possessed by the PROVIDER" the PROVIDER asks that the RECIPIENT agee to the following before the RECIPIENT receives the MATERIAL:

The MATERIAL will be used in accordance with the following contract which RECIPIENT has been awarded by US Department of Health and Human Services: HHSOxxxx. The MATERI.AL will be used by the RECIPIENT for the purpose of the research, development and manufacture of influenza vaccines for US Department of Health and Human Services. Commercialization of the MATERIAL or vaccine derived from the MATERIAL may require commercialization licenses from extant patent holder(s) of the reverse genetics methodology andlor products obtained using reverse genetics methods.

With the exception of the distribution of the MATERIAL and vaccine derived from the MATERIAL (a) among the RECIPIENT's (or its affiliates') facilities and operations in xxxx(b) to the US Department of Health and Human Services,
which the PROVIDER hereby consents to, the MATERIAL will not be further distributed by the RECIPIENT without the PROVIDER's written consent. The RECIPIENT shall refer to the PROVIDER any request for the MATERIAL by any individual or company outside of the RECIPIENT and its affiliates.

Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. THE PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITIHER EXPRESSED OR IMPLIED. TIHERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Unless prohibited by law, the RECIPIENT assumes all liability for claims for damages.

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Wednesday, November 26, 2008 3:05 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: RE: MTA

Thanks for the quick follow up. Tim is excited about this. Here's a note from him: All my contact has been with Janice Knight in Tech Transfer. She's spoken with their OGC but I have not.

While I'm at it, in anticipation of a successful resolution of the dilemna and perhaps as a test case would you be willing to ship us your A/Chicken/India/NIV33407/2006? Also, the list we saw said the FDA had A/Duck/Laos/3295/2006. I didn't think FDA made these. Is this yours?

(b)(4)

Thanks again,
Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,
Swiftwater, PA.18370
570-957-2513

From: Donis, Ruben O. (CDC/CCID/NCIRD)
To: 'Richard.Hjorth@sanofipasteur.com'
Cc: Shaw, Michael (CDC/CCID/NCIRD); Cox, Nancy (CDC/CCID/NCIRD)
Sent: Tue Nov 25 22:42:15 2008
Subject: FW: MTA
Hi Richard,
I see your point. I think we are moving towards CDC providing rg-derived vaccine candidates to manufacturers without any use restrictions – CDC will simply ask for waivers of liability and inform recipients that they are reponsible for compliance with IP laws.

I am copying Michael Shaw and Nancy Cox who have been in discussions about updating the MTA – not sure if the CDC legal folks are going to embrace this liberal approach.

Best regards,
Ruben

From: Richard.Hjorth@sanofipasteur.com [mailto:Richard.Hjorth@sanofipasteur.com]
Sent: Tuesday, November 25, 2008 10:11 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: FW: MTA

Hi Ruben,
I wonder if I can enlist your help with a mutually beneficial endeavor. One of our senior lawyers, Tim Howe, has been trying to work on this with some CDC lawyers and they don't seem to be getting very far. The issue is that you are making pre-pandemic vaccine viruses but right now, there are too many restrictions on their use in the CDC Simple Letter Agreements for them to be of much use to us. We would like to be able to use these strains to make commercial vaccines and to make donations to WHO. We've already commited as a company to donate to WHO.
We already have worked out an agreement with (b)(4) that allows us to do all these things. Perhaps this could be a model for a similar CDC agreement.
I am hoping you might know the right people to speak with that may be able to move this along. I would hate to have to ask the NIBSC to make the same viruses you have already made just so we can use them. As you know, we already have an agreement with (b)(4) to use their reverse genetics so that should not be a concern.
Thanks for any help you can provide.
Rich

Richard Hjorth, Ph.D.
Director, Viral Technology
sanofi pasteur,
Discovery Drive,
Swiftwater, PA.18370
570-957-2513

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, January 07, 2009 8:03 AM
To: Foster, Joseph A. (CDC/OCOO/OD)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: Commercialization of Reverse Genetics Influenza Reassortants

Joe,

No, I haven't heard anything. I really don't see why we don't treat these as any other CDC intellectual property and move forward accordingly. One of the outstanding issues is just how much reach through does (b)(4) have on products created using reverse genetics techniques. I do not know how to get the program to respond to the question of licensing the RG products, nor am I completely sure who would make the decision, i.e., Nancy Cox as the Division Director or Anne Schuchat as the Center Director. I don't perceive this as a burning issue for them.

Were you able to discuss the issues with anyone at NIH to find out their approach, if any?

Janice

(b)(5)

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, October 29, 2008 8:18 AM
To: Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Cc: Horton, Heather H. (CDC/OCOO/OD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: Commercialization of Reverse Genetics Influenza Reassortants
Importance: High

Andrew, Joe, Heather,

I know you are all very, very busy, but I have tried to get an answer to Sanofi Pasteur's (SP) issues regarding commercialization of the Influenza Reverse Genetics reassortants and/or derivatives. SP brought this to my attention in July and I still can't provide Tim Howe an answer. If possible could you participate in a conference call with Lisa and myself? I have attached the MTA and Amendment #1 (pdf) SP signed to receive the reassortants as well as a proposed draft MTA from SP for CDC review. Please provide me with times you will have free and any further background

information you may want to have prior to the call. Also, if you feel anyone from the Influenza Division or NCIRD, please provide their names.

Thanks,

Janice

From: Tim.Howe@sanofipasteur.com [mailto:Tim.Howe@sanofipasteur.com]
Sent: Tuesday, October 28, 2008 1:14 PM
To: Knight, Janice (CDC/CCID/OD)
Cc: James.Matthews@sanofipasteur.com; William.Harris@sanofipasteur.com
Subject: RE: MTA

Dear Janice,

Just another reminder that we are most eager to talk to CDC about the current form of MTA that has been used to access pre-pandemic seed strains. have you had any feedback from your attorneys yet? We truly feel a sense of urgency around this topic and I would very much appreciate hearing from you soon. I have put in copy Dr. James Matthews, a Sr Director in our Public Policy office in DC responsible overall for all of our pre-pandemic contracting activities, and Mr. William Harris, an attorney in our Swiftwater office responsible for supporting the US govt contracting efforts, as I would like to suggest that we arrange a meeting as soon as possible where Jim and I, and possibly Bill, would go to CDC to meet with your team and share our goals and objectives.

Timothy R. Howe, Ph.D.
Assoc. Vice President & Asst. General Counsel,
R&D and Business Development
Sanofi pasteur
2 avenue pont Pasteur
Lyon 69007 France
Tel: 04 3737 7515
Fax: 04 3737 7061
Mobile: (b)(4),(b)(6)

with kind regards,

Tim Howe

From: Howe, Tim (sanofi pasteur)
Sent: jeudi 11 septembre 2008 19:09
To: Knight, Janice (CDC/CCID/OD)
Subject: RE: MTA

Dear Janice,

Just following up again to see whether you had found the opportunity to discuss these issues with your colleagues and superiors at CDC (and, perhaps, HHS). We remain of the view that these issues are critical to pandemic preparedness and so would appreciate whatever you could do at your end to facilitate a conversation, if not a meeting, with the right people within CDC.

Thanks in advance for your help.

Tim Howe

From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
Sent: jeudi 17 juillet 2008 19:12
To: Howe, Tim (sanofi pasteur)
Subject: RE: MTA

Dear Dr. Howe,

Thank you for your prompt response. I have initiated discussions with our patent attorney and I hope to hear from him soon. I will follow-up with you as soon as possible.

Janice

Janice C. Knight

Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Tim.Howe@sanofipasteur.com [mailto:Tim.Howe@sanofipasteur.com]
Sent: Thursday, July 17, 2008 9:49 AM
To: Knight, Janice (CDC/CCID/OD)
Subject: MTA

Dear Ms. Knight,

I just left you a voice mail in an attempt to follow up on a voice mail I left you some weeks ago. This time of year can be especially challenging.

Our scientists, including our Principle Investigator, Richard Hjorth, have received reference seeds in the past from Ruben Donis. See, for example, Simple Letter Agreement, CDC Reference No. FLU-06-003-01, wherein we obtained Influenza A virus reassortant Anhui/01/2005 (H5N1)-PR8-IBCDC-RG6 Reference Strain, in which agreement we were given the right to use the reference A/Anhui seed in furtherance of US govt contracting as well as for internal research and for immunization of our critical workforce, but not for commercial use.

Can you tell from your records whether we received the Bar-Headed Goose reference seed from CDC and, if so, under what conditions? As you are aware, we have a full commercialization license with MedImmune (with the limited exceptions that we cannot make NS-1 deletions or live attenuated flu vaccines) and we are getting requests from foreign governments for pre-pandemic vaccine for stockpiling purposes and would like to amend as necessary any previous MTAs with CDC to give us the "full bundle of rights".

I look forward to discussing this with you in the very near term. There is some sense of urgency around this issue, as our window of opportunity for producing pre-pandemic vaccine will close shortly.

With best regards,

Tim Howe

Timothy R. Howe, Ph.D.
Assoc. Vice President & Asst. General Counsel,
R&D and Business Development
Sanofi pasteur
2 avenue pont Pasteur
Lyon 69007 France
Tel: 04 3737 7515
Fax: 04 3737 7061
Mobile: (b)(4),(b)(6)

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Friday, December 12, 2008 10:02 AM
To: Watkins, Andrew (CDC/OD/OCSO); Donis, Ruben O. (CDC/CCID/NCIRD)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Has a decision been made regarding the CSL receipt of the A/Anhui RG6 virus yet with regard to potential commercial use of the material for production of a stockpile of vaccine? Just as a reminder, we allowed several Japanese firms to make a stockpile for the Japanese government using the MTA only.

Janice

From: Watkins, Andrew (CDC/OD/OCSO)
Sent: Monday, December 01, 2008 8:49 AM
To: Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Rubin, for me, I'm fine with either a phone call or in person. My Outlook Calendar is up to date, or just tell us your meeting time preferences.

Andrew

Andrew Watkins
Director, CDC Technology Transfer Office

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Sunday, November 30, 2008 11:23 PM
To: Knight, Janice (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Janice,
I agree that the << "THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS". >> should stay. This refers to the virus we provide, which has not been tested for absence of any adventitious agents, etc. However, if the recipient generates and qualifies a seed virus under a process that persuades a regulatory body to grant an IND permit to use in human clinical trials, they are OK. Therefore the proposed << The Research Material will be use to generate from progeny virus under GMP conditions seed virus for production of pilot lots of inactivated candidate vaccines for use in human clinical trials.>> looks fine to me.

Andrew, Lisa, Janice,
I would like to talk to you about "commencial use" queries from CSL and others. Phone call or in person?

Thanks,
Ruben

From: Knight, Janice (CDC/CCID/OD)
Sent: Monday, November 24, 2008 10:43 AM
To: Watkins, Andrew (CDC/OD/OCSO); Donis, Ruben O. (CDC/CCID/NCIRD)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05
Importance: High

Hi Andrew, Ruben,

I have attached the latest draft of the Pre-approved MTA for the transfer of the Anhui avian influenza reverse genetics reassortant to CSL, Limited, Australia. CSL requested some minor changes which have been made, but I want to confirm that my assessment of the situation is correct. If you recall, earlier this year, at the suggestion of Dale Berkely we replaced the pre-approved MTA template with a template that was very nearly the same as our standard MTA template which removes references to (b)(4) Also removed in paragraph 3 is the previous menu of possible allowed uses of the Research Material. This menu is replaced with a statement of use requirement to be added in a box under paragraph 3 as is required in the standard template. The requests for the reassortants must originate with Ruben in Influenza to approve the use as it should appear in paragraph 3. The original menu choices were:

a. Generation of virus seed for production of pilot lots of inactivated candidate vaccines for use in human clinical trials.
b. Generation of virus seed for production of pilot lots of inactivated vaccines for use in animals.
c. For in vitro studies to assess immune responses to H5N1 in humans or animals.
d. For in vivo studies in laboratory animals to assess immune responses to H5N1.
e. Other. Please attach a brief description of research project to the agreement.

CSL is concerned with the statement in clause 2, page 2 of the attached draft, which states that "THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS". They ask, "Given that one key purpose of this RG virus candidate is to serve as a potential pre-pandemic vaccine for human use and for clinical studies for vaccine development, I wonder if this clause could be modified." I propose to add the following to paragraph 3 to clarify the allowable use for human clinical trials:

The Research Material will be use to generate from progeny virus under GMP conditions seed virus for production of pilot lots of inactivated candidate vaccines for use in human clinical trials.

I believe CSL performs clinical trials themselves and I have asked Influenza to find out if their use of this material would constitute any commercial purpose.

****PS Has any information come down regarding the use of the reverse genetics reassortants or derivatives for commercial purposes?

Janice
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Peter.Schoofs@csl.com.au
To: Hoelscher, Mary (CDC/CCID/NCIRD)
Sent: Thu Oct 30 21:50:39 2008
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hello Mary,

An issue has been identified in the MTA following review by our IBC delegate.

She notes that clause 2, page 2, states that "THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS".

Given that one key purpose of this RG virus candidate is to serve as a potential pre-pandemic vaccine for human use and for clinical studies for vaccine development, I wonder if this clause could be modified.

I can understand that the samples of material should not be permitted to go into patients as these may not have been prepared under GMP systems and there is no claim that they are fit for any purpose, however vaccine produced from progeny virus under GMP conditions should be able to be used in human clinical studies or for preparation of pre-pandemic vaccine.

If the research materials were defined as the samples of the virus supplied and also define progeny then perhaps the clause could be modified to indicate that progeny virus may be used to prepare inactivated vaccine for use in human subjects (subject to provisions of a quality manufacturing / GMP system) as intended.

I note that the earlier MTA in place for A/Indonesia/5/05 RG candidate specified use in the clinical setting.

Perhaps you can see a way past this conundrum.

Regards

Peter

Peter Schoofs

Manager,

Influenza Development, R&D

CSL Limited

Ph +61 3 9389 1585

Fax +61 3 9381 1913

Email: Peter.schoofs@csl.com.au

From: Hoelscher, Mary (CDC/CCID/NCIRD) [mailto:mzr1@cdc.gov]
Sent: Tuesday, 9 September 2008 12:04 AM
To: Schoofs, Peter AU/PKV
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Peter,

Here is the edited version with the double signatory for CSL. This is the latest version that our Tech Transfer Office has on record. Our MTA was edit in March/April upon suggestions from CDC's legal department. Hopefully we are both working off the same version. Please note that there are 3 boxes left which need to be completed - one in Paragraph 3 describing the Research Project; and 2 on the signature page: Recipient's Biosafety Official and second Authorized Official as CSL requested the addition of a second signatory. Let me know if you have any more questions.

Mary

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Sunday, November 30, 2008 11:23 PM
To: Knight, Janice (CDC/CCID/OD); Watkins, Andrew (CDC/OD/OCSO)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Janice,
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I would like to talk to you about "commencial use" queries from CSL and others. Phone call or in person?

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Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
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Janice
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Peter.Schoofs@csl.com.au
To: Hoelscher, Mary (CDC/CCID/NCIRD)
Sent: Thu Oct 30 21:50:39 2008
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

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Perhaps you can see a way past this conundrum.

Regards

Peter

Peter Schoofs

Manager,

Influenza Development, R&D

CSL Limited

Ph +61 3 9389 1585

Fax +61 3 9381 1913

Email: Peter.schoofs@csl.com.au

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Sent: Tuesday, 9 September 2008 12:04 AM
To: Schoofs, Peter AU/PKV
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Peter,

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Mary

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Blake-DiSpigna, Lisa (CDC/CCID/OD)
Sent: Friday, November 28, 2008 9:50 AM
To: Watkins, Andrew (CDC/OD/OCSO); Foster, Joseph A. (CDC/OCOO/OD)
Subject: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Importance: High

fyi...

Janice is working on this particular request. I'm not sure if she had an opportunity to follow up with you. If not, you may hear from her next week.

From: Hoelscher, Mary (CDC/CCID/NCIRD)
Sent: Thursday, November 27, 2008 1:08 PM
To: Knight, Janice (CDC/CCID/OD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: Fw: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05
Importance: High

Responses to the commercial use of a reassortnat virus.

Sent from my BlackBerry Wireless Handheld

From: Peter.Schoofs@csl.com.au
To: Hoelscher, Mary (CDC/CCID/NCIRD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Sent: Thu Nov 27 01:19:06 2008
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05
Hello Mary,

There is no clinical trial planned for this virus at present, though there could be in the future.
CSL has been trying to obtain and prepare working virus seed lots for all of the WHO recommended potential pandemic vaccine strains as a first step in our pandemic preparedness program.
Hence the request for the MTA to allow use in humans. Preparation of working virus seed lots for potential human use in a pandemic response would not constitute a commercial use until / unless a pandemic occurred.

However in the last few days we have been asked by the Australian Government to tender for preparation of material for a pandemic stockpile.
We are considering using the RG version of A/Anhui/1/05 for this stockpile. If used, this would definitely constitute a commercial use of this material.
CSL already holds a licence for commercial applications with the owners of the IP i.e. MedImmune.

CSL is keen to implement MTA's for all potential pandemic vaccine RG strains prepared at CDC. These would all have the potential to be used in human studies or for pandemic response applications.

We would like to receive the RG virus and prepare a working virus seed lot for the A/Anhui RG strain, ideally before Christmas.
Is there any chance that an MTA permitting preparation of a working seed for potential use in humans could be agreed to in the near future?

Thanks
Peter

Peter Schoofs

Manager,
Influenza Development, R&D
CSL Limited

Ph +61 3 9389 1585
Fax +61 3 9381 1913
Email: Peter.schoofs@csl.com.au

From: Hoelscher, Mary (CDC/CCID/NCIRD) [mailto:mzr1@cdc.gov]
Sent: Tuesday, 25 November 2008 2:17 AM
To: Schoofs, Peter AU/PKV
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD)
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Peter,

A couple of questions: Who is sponsoring the clinical trial to evaluate this reassortant as a pandemic vaccine? Does your participation in this clinical trial constitute a commercial use of this material, progeny or derivative?

Mary

From: Peter.Schoofs@csl.com.au [mailto:Peter.Schoofs@csl.com.au]
Sent: Thursday, October 30, 2008 9:51 PM
To: Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hello Mary,

An issue has been identified in the MTA following review by our IBC delegate.

She notes that clause 2, page 2, states that "THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS".

Given that one key purpose of this RG virus candidate is to serve as a potential pre-pandemic vaccine for human use and for clinical studies for vaccine development, I wonder if this clause could be modified.
I can understand that the samples of material should not be permitted to go into patients as these may not have been prepared under GMP systems and there is no claim that they are fit for any purpose, however vaccine produced from progeny virus under GMP conditions should be able to be used in human clinical studies or for preparation of pre-pandemic vaccine.

If the research materials were defined as the samples of the virus supplied and also define progeny then perhaps the clause could be modified to indicate that progeny virus may be used to prepare inactivated vaccine for use in human subjects (subject to provisions of a quality manufacturing / GMP system) as intended.

I note that the earlier MTA in place for A/Indonesia/5/05 RG candidate specified use in the clinical setting.

Perhaps you can see a way past this conundrum.

Regards
Peter

Peter Schoofs
Manager,
Influenza Development, R&D
CSL Limited

Ph +61 3 9389 1585
Fax +61 3 9381 1913
Email: Peter.schoofs@csl.com.au

From: Peter.Schoofs@csl.com.au [mailto:Peter.Schoofs@csl.com.au]
Sent: Thursday, August 28, 2008 2:57 AM
To: Hoelscher, Mary (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hello Mary,

I am resending this email in case it failed to get through or has otherwise been misplaced.
Could you reply to this email to confirm receipt please?

Are there any issues with the requested amendments to the MTA listed below?

Regards
Peter

Peter Schoofs
Manager,
Influenza Development, R&D
CSL Limited

Ph +61 3 9389 1585
Fax +61 3 9381 1913
Email: Peter.schoofs@csl.com.au

Hello Mary,

CSL is still keen to implement an MTA with CDC for transfer of the RG candidate vaccine strain for A/Anhui/1/05.
There was a draft MTA that was initially reviewed, some changes requested and implemented in a second version of the draft MTA.
However, in edition 2 there were other changes made to the MTA and these were requested to be re-instated as per the correspondence below.

Could you give me an update on the status of the MTA please?
Is edition 3 available for review and hopefully execution?

Thanks for any help you may be able to give.

Regards
Peter

Peter Schoofs
Manager,
Influenza Development. R&D
CSL Limited

Ph +61 3 9389 1585
Fax +61 3 9381 1913
Email: Peter.schoofs@csl.com.au

Hello Mary,

I have been asked by CSL's legal department to have two amendments made to the MTA and a change to the signatory names.

They are:
1. Clause 4 - Insert the following words after "disclosed to Recipient wihout a confidentiality obligation" -
"or that the Recipient can establish by reasonable proof is independently developed by employees of the Recipient who had no knowledge of the confidential information disclosed."

From: Hoelscher, Mary (CDC/CCID/NCIRD) [mailto:mzr1@cdc.gov]
Sent: Tuesday, 9 September 2008 12:04 AM
To: Schoofs, Peter AU/PKV
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Peter,

Here is the edited version with the double signatory for CSL. This is the latest version that our Tech Transfer Office has on record. Our MTA was edit in March/April upon suggestions from CDC's legal department. Hopefully we are both working off the same version. Please note that there are **3 boxes** left which need to be completed - one in **Paragraph 3** describing the Research Project; and 2 on the **signature page**: Recipient's Biosafety Official and second Authorized Official as CSL requested the addition of a second signatory. Let me know if you have any more questions.

Mary

From: Peter.Schoofs@csl.com.au [mailto:Peter.Schoofs@csl.com.au]
Sent: Monday, September 08, 2008 1:03 AM
To: Hoelscher, Mary (CDC/CCID/NCIRD)
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Selina.Sawaya@csl.com.au
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hi Mary,

I look forward to receiving the modified MTA.
We do still require 2 authorized signatories please.

Regards
Peter

Peter Schoofs
Manager,
Influenza Development, R&D
CSL Limited

Ph +61 3 9389 1585
Fax +61 3 9381 1913
Email: Peter.schoofs@csl.com.au

From: Hoelscher, Mary (CDC/CCID/NCIRD) [mailto:mzr1@cdc.gov]
Sent: Saturday, 6 September 2008 7:25 AM
To: Schoofs, Peter AU/PKV
Cc: Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Peter,

Tech Transfer is modifying clause 4 but have said that changes to clause 5 are not acceptable as execution is the effective date (date of the last authorized signatory) and not when shipment occurs. I had hoped to have the modified agreement before the end of today, but it has not been sent and their office is closed. I should have the document Monday to forward to you.

Do you still need 2 signatories for CSL?

Sorry for the delay.

Mary

2. Clause 5 - After "three (3) years have elapsed", insert "*from receipt of Research Materials*".

Note: These phrases were present in the previous draft of the MTA reviewed by CSL.

In addition, in the signing clause, "Edward Bailey, Assistant Company Secretary" should be replaced with "Peter Turvey, Company Secretary".

Could these amendments be made to the MTA and the new version returned to me for completion and approval?

Regards
Peter

Peter Schoofs
Manager,
Influenza Development, R&D
CSL Limited

Ph +61 3 9389 1585
Fax +61 3 9381 1913
Email: Peter.schoofs@csl.com.au

From: Sawaya, Selina AU/PKV
Sent: Friday, 8 February 2008 11:40 AM
To: Schoofs, Peter AU/PKV
Subject: FW: TRIM: RE: TRIM: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hi Peter,

As discussed with you earlier today, I have set out below the changes we need to request from CDC as these were in the previous version we had reviewed:

1. Clause 4 - Insert the following words after "disclosed to Recipient without a confidentiality obligation" -

"or that the Recipient can establish by reasonable proof is independently developed by employees of the Recipient who had no knowledge of the confidential information disclosed."

2. Clause 5 - After "three (3) years have elapsed", insert "*from receipt of Research Materials*".

In addition, in the signing clause, "Edward Bailey, Assistant Company Secretary" should be replaced with "Peter Turvey, Company Secretary".

Regards,

Selina Sawaya
Legal Consultant
CSL Limited

45 Poplar Road, Parkville | VIC 3052 | Australia
phone +613 9389 2735 | fax +613 9387 8454
selina.sawaya@csl.com.au
www.csl.com.au

From: Sawaya, Selina AU/PKV
Sent: Thursday, 7 February 2008 5:16 PM
To: Schoofs, Peter AU/PKV
Subject: TRIM: RE: TRIM: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hi Peter,

I note that this version of the MTA is slightly different to the version I reviewed in July 2007. I would like to make some amendments to the MTA to bring it into line with the previous version we reviewed. Since I can't make amendments to the MTA sent to me (it doesn't allow me to make changes), can you please request a version from CDC that we can amend.

Regards,

Selina Sawaya
Legal Consultant
CSL Limited

45 Poplar Road, Parkville | VIC 3052 | Australia
phone +613 9389 2735 | fax +613 9387 8454
selina.sawaya@csl.com.au
www.csl.com.au

From: Schoofs, Peter AU/PKV
Sent: Tuesday, 5 February 2008 11:10 AM
To: Sawaya, Selina AU/PKV
Subject: TRIM: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hello Selina,

I have received an edited MTA for Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG5 Reference Strain from CDC.
I have completed the required fields and would like to progress approval of the MTA **if the revised document is acceptable**. (Attached).

Note, CDC has made a number of changes to the document in addition to the ones that CSL requested.

Please feel free to contact me on X1585

Regards
Peter

Peter Schoofs
Manager,
Influenza Development, R&D
CSL Limited

Ph +61 3 9389 1585
Fax +61 3 9381 1913
Email: Peter.schoofs@csl.com.au

From: Hoelscher, Mary (CDC/CCID/NCIRD) [mailto:mzr1@CDC.GOV]
Sent: Tuesday, 6 November 2007 7:43 AM
To: Schoofs, Peter AU/PKV
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); McNeill, Valerie (CDC/CCID/OD) (CTR)
Subject: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Dr, Schoofs,

I have replaced Marty Monroe as the MTA liaison for the Influenza Division at CDC. Marty had discussed your proposed changes with the Technology Transfer Office (TTO) and they have modified the MTA template to include a second signing clause. However, TTO felt the changes to Clause 5 were unwarranted.

Attached above is the Materials Transfer Agreement (MTA) established by the Centers for Disease Control and Prevention for Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG5 Reference Strain and

modified to meet the requirements of CSL Limited. This MTA assumes that the document is accepted without any additional changes. Please follow the instructions in the letter to Prospective Recipients (attached) as to how to submit the MTA. Note that if your institution has any edits or changes to this agreement, the MTA will then go through the standard CDC-MTA process which may require longer for review, agreement on changes, and subsequent signatures. Upon receipt of the signed MTA, CDC will ship the virus as soon as possible, provided the necessary import permits are enclosed (e.g., shipments to addresses within the USA require a USDA permit).

Thank you for your time and attention to this important matter. Please do not hesitate to contact any of us of at the e-mail addresses or telephone numbers below, should you need more information.

Kind regards,

Mary

Mary (Renshaw) Hoelscher
Center for Disease Control and Prevention
Influenza Division
1600 Clifton Rd
MS:G16
Atlanta, GA 30333
phone 404-639-5446
fax 404-639-2334
mhoelscher@cdc.gov

-----Original Message-----
From: Monroe, Marty (CDC/CCID/NCPDCID)
Sent: Wednesday, October 10, 2007 1:22 PM
To: Knight, Janice (CDC/CCID/OD)
Cc: Hoelscher, Mary (CDC/CCID/NCIRD); 'peter.schoofs@csl.com.au'; Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Janice,
I forwarded Dr. Schoofs' e-mail to you on 8-10-07 asking if the changes below could be made to the pre-approved template to satisfy CSL. I forgot to follow up on this one prior to my departure from Influenza. Can you advise whether these changes are permissible - or possibly whether they are worth the effort if the document must be reviewed by MedImmune subsequent to any changes.
Marty

-----Original Message-----
From: Peter.Schoofs@csl.com.au [mailto:Peter.Schoofs@csl.com.au]
Sent: Thursday, August 09, 2007 9:08 PM
To: Monroe, Marty (CDC/CCID/NCIRD)
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hello Marty,

I have been asked by CSL's legal department to have two amendments made to the MTA.

They are:

1. Clause 5 - The words "his or her" in line 4 to be deleted and replaced with "the Recipient's".

2. A second signing clause for CSL to be inserted. (CSL has 2 authorized signatories for agreements)

Could these amendments be made to the MTA and the new version returned to me for completion and approval?

Regards
Peter

Peter Schoofs
Manager,
Influenza Development, R&D
CSL Limited

Ph +61 3 9389 1585
Fax +61 3 9381 1913
Email: Peter.schoofs@csl.com.au

-----Original Message-----
From: Monroe, Marty (CDC/CCID/NCIRD) [mailto:mcm1@CDC.GOV]
Sent: Tuesday, 3 July 2007 6:41 AM
To: Schoofs, Peter AU/PKV
Subject: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Obviously something happened to your address the first time around so trying again.
Marty

-----Original Message-----
From: Monroe, Marty (CDC/CCID/NCIRD)
Sent: Monday, July 02, 2007 4:35 PM
To: 'Peter.'
Cc: 'Steve.Rockman@csl.com.au'; McNeill, Valerie (CDC/CCID/OD) (CTR); Hicks, Marie (CDC/CCID/NCIRD); Donis, Ruben O. (CDC/CCID/NCIRD)
Subject: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Dear Dr. Schoofs,

Attached above is the Materials Transfer Agreement (MTA) established by the Centers for Disease Control and Prevention for Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG5 Reference Strain. This MTA assumes that the document is accepted without changes. Please follow the instructions in the letter to Prospective Recipients (attached) as to how to submit the MTA. Note that if your institution has any edits or changes to this agreement, the MTA will then go through the standard CDC-MTA process which may require longer for review, agreement on changes, and subsequent signatures. Upon receipt of the signed MTA, CDC will ship the virus as soon as possible, provided the necessary import permits are enclosed (e.g., shipments to addresses within the USA require a USDA permit).

Thank you for your time and attention to this important matter. Please do not hesitate to contact any of us of at the e-mail addresses or telephone numbers below, should you need more information.

Kind regards,
Marty

Marty Monroe, M.P.H.
Program Analyst, Influenza Division
NCIRD/CCID/CDC
MMonroe@cdc.gov
+404-639-1704

Marie Hicks, M.S.
Public Health Advisor, Influenza Division NCIRD/CCID/CDC MHicks@cdc.gov
+404-639-4973

Ruben Donis, Ph.D.
Chief, Molecular Virology and Vaccines Branch, ID NCIRD/CCID/CDC RDonis@cdc.gov
+404-639-4968

-----Original Message-----
From: Donis, Ruben O. (CDC/CCID/NCIRD)

Sent: Thursday, June 28, 2007 9:01 PM
To: 'Peter.Schoofs@csl.com.au'; Monroe, Marty (CDC/CCID/NCIRD)
Cc: 'Steve.Rockman@csl.com.au'
Subject: Re: MTA for RG candidate vaccine strain for A/Anhui/1/05

Dear Peter,
Sorry for the oversight, happy to help.

Marty,
Please see the request below.

Best,
Ruben

Sent from my BlackBerry Wireless Handheld

-----Original Message-----
From: Peter.Schoofs@csl.com.au <Peter.Schoofs@csl.com.au>
To: Donis, Ruben O. (CDC/CCID/NCIRD)
CC: Steve.Rockman@csl.com.au <Steve.Rockman@csl.com.au>
Sent: Thu Jun 28 20:50:36 2007
Subject: MTA for RG candidate vaccine strain for A/Anhui/1/05

Hello Ruben,

I am resending this message for two reasons;

* Firstly in case you were away last week at the influenza options meeting in Toronto
* Secondly, to ask that you copy any emails to Steve Rockman (email link above)

Regards

Peter

Hello Ruben,

I understand that CDC has made an RG candidate vaccine strain for the clade 3 influenza virus A/Anhui/1/05.

I would like to initiate an MTA to receive this virus comparable to the MTA established for Indo/5-PR8-RG2. (MTA reference FLU-06-085).

Regards

Peter

Peter Schoofs

Manager - Influenza Development, R&D

CSL Limited

45 Poplar Road

Parkville

Melbourne

Victoria

Australia

3052

Ph +61 3 9389 1585

Fax +61 3 9381 1913

From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Wednesday, October 11, 2006 5:06 PM
To: Balish, Amanda (CDC/CCID/NCIRD); Mabry, Jan (CDC/CCID/NCIRD)
Cc: Matsuoka, Yumi (CDC/CCID/NCIRD); Hicks, Marie (CDC/CCID/NCIRD); Monroe, Marty (CDC/CCID/NCIRD)
Subject: FW: Fully Executed Influenza MTA with CDC Reference No.
FLU-06-085

Jan and Amanda,

Please send Dr. Peter Schoofs one vial of the A/Indonesia/5/05-PR8 reassortant Indo/05/2005(H5N1)/PR8-IBCDC-RG2 (also referred to as
Ind05/PR8-RG2 for brevity) GLP stock that has CDC ID number 2006716817;
C1/E2 HA:1024.

His contact information is in the attached MTA and the email below.

Thank you very much for your help.

Ruben

Ruben Donis, PhD

Molecular Virology and Vaccines Branch

Influenza Division, NCIRD, CCID

Centers for Disease Control and Prevention

1600 Clifton Road - Mail Stop G-16

Atlanta, GA 30333

Phone: (404) 639-4968

Fax: (404) 639-2334

From: Hicks, Marie (CDC/CCID/NCID)
Sent: Monday, October 02, 2006 10:18 AM
To: Donis, Ruben O. (CDC/CCID/NCID)
Cc: Thomas, Stephanie (CDC/CCID/NCID) (CTR)
Subject: FW: Fully Executed Influenza MTA with CDC Reference No. FLU-06-085

Hi Ruben--Can you answer the question about when this might be shipped?
It's a pre-approved MTA FLU-06-085 and we got approval from Glenda to ship on September 7 (with all signatures on hard copy being final 9/27).
Thanks!

Marie

From: Thomas, Stephanie (CDC/CCID/NCID) (CTR) [mailto:sqt8@cdc.gov]
Sent: Saturday, 30 September 2006 1:02 AM
To: Crowley, Jayne AU/PKV
Cc: Blake-DiSpigna, Lisa (CDC/CCID/NCID)
Subject: Fully Executed Influenza MTA with CDC Reference No. FLU-06-085

<<FLU-06-085 CSL Limited.pdf>>

Jayne,

As follow-up to your telephone inquiry to Lisa Blake-Dispigna regarding the aforementioned MTA, attached is a scanned copy of the fully executed FLU MTA between CSL Limited and CDC. An original hardcopy was sent to your attention via FedEx on September 27, 2006. The FedEx tracking number for this envelope is 791557187788.

Please do not hesitate to contact me if you have any additional questions or concerns regarding this Agreement.

Best Regards,

Stephanie Thomas
Amer Technology Consultant
Technology Transfer
Coordinating Center for Infectious Diseases 1600 Clifton Road N.E. Mailstop A-42 Atlanta, GA 30322
404-639-2681
404-638-5475

Act 1988 (Cth).

If you are not an intended recipient, please contact us at once by return email and then delete both messages.

CSL Limited A.C.N. 051 588 348

45 Poplar Road Parkville Victoria 3052 Australia

Phone: +61 3 9389 1911 Fax: +61 3 9389 1434

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45 Poplar Road Parkville Victoria 3052 Australia

Phone: +61 3 9389 1911 Fax: +61 3 9389 1434

****

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Wednesday, November 26, 2008 1:21 PM
To: 'Blayer, Simone'
Cc: Watkins, Andrew (CDC/OD/OCSO)
Subject: RE: another point of discussion

Dear Simone,

As to your question regarding use of the RG reassortants outside/beyond HHS contracts, I currently do not have that information. I have cc'd Dr. Andrew Watkins, Director of Technology Transfer Office for CDC for his comment.

Regards,

Janice

Janice C. Knight

Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Blayer, Simone [mailto:simone.blayer@novartis.com]
Sent: Wednesday, November 26, 2008 12:44 PM
To: Knight, Janice (CDC/CCID/OD)
Subject: another point of discussion

Dear Janice,
I have also a different question: I would also like to understand what needs to be in place in order to use, in a future time, the RG strains of CDC also for applications outside / beyond the HHS contracts.

We have negotiated IP rights with the company patenting the RG technology already (b)(4) I would like to understand which kind of documentation you would need in order to clear this option. Shall we need a brand new MTA? Do you need HHS or Novartis statemnets that an agreement has been reached?
Please let me know.
Thanks
Simone

Simone Blayer
TechOps Influenza Franchise
Novartis Vaccines and Diagnostics GmbH & Co. KG
Emil-von-Behring-Str. 76
35041 Marburg/Germany
M: (b)(4),(b)(6)

T: +49 (0) 6421-39 4456
F: +49 (0) 6421-39 3666
simone.blayer@novartis.com

From: Blayer, Simone
Sent: Mittwoch, 26. November 2008 16:20
To: 'Knight, Janice (CDC/CCID/OD)'
Cc: 'Donis, Ruben O. (CDC/CCID/NCIRD)'
Subject: Novartis MTA
Importance: High

Dear Janice,
Thank you for the nice conversation we had today. In reference to the Novartis MTAs, I need to apologise to you because the situation is different from what I communicated:

1. We would like to have in Novartis Marburg the strain A/Anuhi RG-6.
2. We have an MTA signed with Novartis for this strain, based on HHS contract for Stockpile of Anhui: HHS0100200700028I. This MTA (I include a copy and its amendment) is in place.
3. The point is that **the HHS contract upon which we will used the A/Anuhi RG-6 in Marburg is another one: it is HHS Phase III Optaflu: HHSO100200700030C**.

For this reason I believe I might need an additiona MTA on the basis of the exhisting one that I could make sign and deliver to you.
I hope this is the correct way to move forward. If so, please send me the form, I will have it signed by the Novartis head and then send it back to you, so that signatures can be done. I hope this is the fastest way.

Many thanks and kind regards,
Simone

Simone Blayer
TechOps Influenza Franchise
Novartis Vaccines and Diagnostics GmbH & Co. KG
Emil-von-Behring-Str. 76
35041 Marburg/Germany
M: (b)(4),(b)(6)
T: +49 (0) 6421-39 4456
F: +49 (0) 6421-39 3666
simone.blayer@novartis.com

From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
Sent: Mittwoch, 26. November 2008 15:21
To: Blayer, Simone
Cc: Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Hoelscher, Mary (CDC/CCID/NCIRD);

Blake-DiSpigna, Lisa (CDC/CCID/OD); Pannatier, Serge; Ryoko Krause; Trusheim, Heidi
Subject: RE: Funding of IFPMA / CDC research activities
Importance: High

Dear Simone,

I have attached a final draft (Grant Letter NCIRD-G095066-00 IFPMA-09 DonisKlimov clean.doc) of the proposed subaward for IFPMA signature. I have accepted your changes to the initial draft sent to you by me on October 3rd. However, I have added language to term 1 and 2, and deleted a sentence from term 4. For your convenience, I have attached a track changes document (Grant Letter IFPMA-09 DonisKlimov v 20Nov08.doc) to highlight these changes.

If you are in agreement with this final draft, please print this letter on IFPMA letterhead, have signed by the Director General of IFPMA and courier it to me at the address below. Upon receipt of your signed letter, I will send forward for final CDC processing.

Thank you,

Janice

Janice C. Knight
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Blayer, Simone [mailto:simone.blayer@novartis.com]
Sent: Tuesday, October 28, 2008 2:53 PM
To: Knight, Janice (CDC/CCID/OD); Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Trusheim, Heidi
Cc: Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD); Pannatier, Serge; Ryoko Krause
Subject: Funding of IFPMA / CDC research activities

Dear Janice,
Thank you so much for the very constructive proposal and apologies for this late reply. The sub-award approach is accepted by IFPMA.

Please find enclosed proposal on our side including some points to govern this funding. The budget has been increased to reflect the scientific plan activities.
New points, mainly:

1. joint steering committee of principal investigators
2. donation regulated according to the Swiss statutory rules governing donations
3. research plan included
4. joint publications

We will liaise now in details for points 1,3,4 with Ruben Donis. We are confident that in the course of this coming month we could finalise the agreement.
I look forward to hearing from you in the near future.

Kind regards,
Simone

Simone Blayer
TechOps Influenza Franchise
Novartis Vaccines and Diagnostics GmbH & Co. KG
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M: (b)(4),(b)(6)
T: +49 (0) 6421-39 4456
F: +49 (0) 6421-39 3666
simone.blayer@novartis.com

From: Knight, Janice (CDC/CCID/OD) [mailto:jck1@cdc.gov]
Sent: Freitag, 3. Oktober 2008 17:31
To: Donis, Ruben O. (CDC/CCID/NCIRD); Klimov, Alexander (CDC/CCID/NCIRD); Blayer, Simone; Trusheim, Heidi
Cc: Hoelscher, Mary (CDC/CCID/NCIRD); Blake-DiSpigna, Lisa (CDC/CCID/OD)
Subject: RE: material CRADA

After discussions with Ruben and Lisa, I would like to propose that we use the attached draft letter to govern the funding of this research activity. This is an initial draft and subject to negotiation.

Janice

Janice C. Knight

Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
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From: Donis, Ruben O. (CDC/CCID/NCIRD)
Sent: Monday, August 04, 2008 2:54 PM
To: 'Blayer, Simone'
Cc: Hoelscher, Mary (CDC/CCID/NCIRD); Knight, Janice (CDC/CCID/OD); Driesner, Sue (CDC/CCID/OD) (CTR); Blake-DiSpigna, Lisa (CDC/CCID/OD); 'Trusheim, Heidi'
Subject: RE: material CRADA

Hi Simone,
You are right, the Materials CRADA is not what the Influenza Divison used previously for the egg isolation contract with IFPMA Manufacturers.
Looking at was CDC will do:

1) Isolate influenza from 20 primary clinical specimen in ATCC MDCK
2) receive ~ 120 isolates from IFPMA Vaccine Manufacturers (20 primary strains: amplified in 6 different cell systems)
3) sequence and antigenic analysis of 120 viruses

We discussed this project with CDC TTO. To expedite processing, CDC TTO suggested a MCRADA contract. I see your points – I'm not sure if we can add provisions to this MCRADA or we should consider starting with a CRADA template like the one used for the egg isolation. See a template attached.
Thanks,
Ruben

From: Blayer, Simone [mailto:simone.blayer@novartis.com]
Sent: Monday, August 04, 2008 2:10 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD); Trusheim, Heidi
Subject: material CRADA

Hi Ruben and Heidi,
Thank you for the call on Friday. I will issue minutes this week.
I had a look at the Material CRADA I received from Heidi, and here I need some guidance:
- there is no scope of this agreement
- there is no financial agreements between the parties
- all other agreements except this one are void once we sign this (more or less).

Is this the right document? Ruben, your input here is required since I would need to push it through the IFPMA lawyer and possibly some company lawyers before it reaches CDC.
Is this what is used for the egg CRADA with IFPMA? I believe the simpler the better in order to avoid very long discussions.
In the case we go ahead with this document, who is the collaborator? This is not TCH, since IFPMA sponsors the study, but samples are received from TCH....
Please let me know and sorry for the questions.
Kind regards,
Simone

Simone Blayer
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simone.blayer@novartis.com

From: Donis, Ruben O. (CDC/CCID/NCIRD) [mailto:rvd6@cdc.gov] ina
Sent: Donnerstag, 31. Juli 2008 00:32
To: Blayer, Simone
Subject: RE: IFPMA CRADA on virus isolation / part of CDC

OK – will stay tuned.
Ruben

From: Blayer, Simone [mailto:simone.blayer@novartis.com]
Sent: Wednesday, July 30, 2008 3:17 PM
To: Donis, Ruben O. (CDC/CCID/NCIRD); Hussain, Althaf

Cc: Trusheim, Heidi; Tsai, Theodore
Subject: RE: IFPMA CRADA on virus isolation / part of CDC

Hi Ruben,
Thank you for the response. I will set up a call for Friday 12-1pm Atlanta time.
Kind regards,
Simone

Simone Blayer
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simone.blayer@novartis.com

From: Donis, Ruben O. (CDC/CCID/NCIRD) [mailto:rvd6@cdc.gov]
Sent: Dienstag, 29. Juli 2008 23:46
To: Blayer, Simone; Hussain, Althaf
Cc: Trusheim, Heidi; Tsai, Theodore
Subject: RE: IFPMA CRADA on virus isolation / part of CDC

Hi Simone,
Sorry for the delay, I was gone and have been catching up in the last few days.
I can talk this week, 12-1 pm Wed, Thurs, or Friday. Friday 11-12 also open.
Best regards,
Ruben

From: Blayer, Simone [mailto:simone.blayer@novartis.com]
Sent: Friday, July 18, 2008 8:50 AM
To: Donis, Ruben O. (CDC/CCID/NCIRD); Hussain, Althaf
Cc: Trusheim, Heidi; Tsai, Theodore
Subject: IFPMA CRADA on virus isolation / part of CDC

Dear Ruben,
I am contacting you following up Heidi's previous contact on a new IFPMA CRADA that we need to advance.
I copy also Althaf Hussein from (b)(4) who will also be a contact person from IFPMA for this purpose.
Heidi is on holidays at the moment and I would like, if possible and you have time, to have a quick talk on the phone on how we could advance this.
We have a budget in place, but I believe the whole admin / contract part still needs to be done, and we need to put a sound scientific plan together.
When could be a suitable day / time for you?
Althaf will be also able to join, he is based on the West Coast.
Many thanks and kind regards,
Simone

Simone Blayer

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simone.blayer@novartis.com

Watkins, Andrew (CDC/OSELS/LSPPPO)

From: Knight, Janice (CDC/CCID/OD)
Sent: Monday, November 24, 2008 10:43 AM
To: Watkins, Andrew (CDC/OD/OCSO); Donis, Ruben O. (CDC/CCID/NCIRD)
Cc: Blake-DiSpigna, Lisa (CDC/CCID/OD); Hoelscher, Mary (CDC/CCID/NCIRD)
Subject: FW: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05
Attachments: CSL-Anhui-RG6 24Nov08.doc

Importance: High

Hi Andrew, Ruben,

I have attached the latest draft of the Pre-approved MTA for the transfer of the Anhui avian influenza reverse genetics reassortant to CSL, Limited, Australia. CSL requested some minor changes which have been made, but I want to confirm that my assessment of the situation is correct. If you recall, earlier this year, at the suggestion of Dale Berkely we replaced the pre-approved MTA template with a template that was very nearly the same as our standard MTA template which removes references to (b)(4) Also removed in paragraph 3 is the previous menu of possible allowed uses of the Research Material. This menu is replaced with a statement of use requirement to be added in a box under paragraph 3 as is required in the standard template. The requests for the reassortants must originate with Ruben in Influenza to approve the use as it should appear in paragraph 3. The original menu choices were:

a. Generation of virus seed for production of pilot lots of inactivated candidate vaccines for use in human clinical trials.
b. Generation of virus seed for production of pilot lots of inactivated vaccines for use in animals.
c. For in vitro studies to assess immune responses to H5N1 in humans or animals.
d. For in vivo studies in laboratory animals to assess immune responses to H5N1.
e. Other. Please attach a brief description of research project to the agreement.

CSL is concerned with the statement in clause 2, page 2 of the attached draft, which states that "THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS". They ask, "Given that one key purpose of this RG virus candidate is to serve as a potential pre-pandemic vaccine for human use and for clinical studies for vaccine development, I wonder if this clause could be modified." I propose to add the following to paragraph 3 to clarify the allowable use for human clinical trials:

The Research Material will be use to generate from progeny virus under GMP conditions seed virus for production of pilot lots of inactivated candidate vaccines for use in human clinical trials.

I believe CSL performs clinical trials themselves and I have asked Influenza to find out if their use of this material would constitute any commercial purpose.

****PS Has any information come down regarding the use of the reverse genetics reassortants or derivatives for commercial purposes?

Janice
Health Scientist, Technology Transfer Specialist
Centers for Disease Control and Prevention
CCID Technology Transfer MS A42
1600 Clifton Road, NE
Atlanta, GA 30333
Phone: 404 639-2679
FAX: 404 638-5465

From: Peter.Schoofs@csl.com.au
To: Hoelscher, Mary (CDC/CCID/NCIRD)
Sent: Thu Oct 30 21:50:39 2008
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Hello Mary,

An issue has been identified in the MTA following review by our IBC delegate.

She notes that clause 2, page 2, states that "THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS".

Given that one key purpose of this RG virus candidate is to serve as a potential pre-pandemic vaccine for human use and for clinical studies for vaccine development, I wonder if this clause could be modified.

I can understand that the samples of material should not be permitted to go into patients as these may not have been prepared under GMP systems and there is no claim that they are fit for any purpose, however vaccine produced from progeny virus under GMP conditions should be able to be used in human clinical studies or for preparation of pre-pandemic vaccine.

If the research materials were defined as the samples of the virus supplied and also define progeny then perhaps the clause could be modified to indicate that progeny virus may be used to prepare inactivated vaccine for use in human subjects (subject to provisions of a quality manufacturing / GMP system) as intended.

I note that the earlier MTA in place for A/Indonesia/5/05 RG candidate specified use in the clinical setting.

Perhaps you can see a way past this conundrum.

Regards

Peter

Peter Schoofs

Manager,

Influenza Development, R&D

CSL Limited

Ph +61 3 9389 1585

Fax +61 3 9381 1913

Email: Peter.schoofs@csl.com.au

From: Hoelscher, Mary (CDC/CCID/NCIRD) [mailto:mzr1@cdc.gov]
Sent: Tuesday, 9 September 2008 12:04 AM
To: Schoofs, Peter AU/PKV
Subject: RE: CSL_MTA for RG candidate vaccine strain for A/Anhui/1/05

Peter,

Here is the edited version with the double signatory for CSL. This is the latest version that our Tech Transfer Office has on record. Our MTA was edit in March/April upon suggestions from CDC's legal department. Hopefully we are both working off the same version. Please note that there are 3 boxes left which need to be completed - one in Paragraph 3 describing the Research Project; and 2 on the signature page: Recipient's Biosafety Official and second Authorized Official as CSL requested the addition of a second signatory. Let me know if you have any more questions.

Mary

PUBLIC HEALTH SERVICE MATERIAL TRANSFER AGREEMENT

To Prospective Recipients;

This Agreement is to be used for the distribution of:

Influenza A virus reassortant Viet/1203/2004(H5N1)/ PR8-IBCDC-RG
Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG6

The intended recipients of this technology are worldwide institutions involved in the diagnosis and research of Influenza infections which can provide adequate assurances that the virus will be handled safely (see appendix A).

This agreement has been approved in advance by the Director, National Center for Infectious Diseases, Centers for Disease Control and Prevention with the following restrictions/rules:

1. In order to ensure **rapid** distribution of the Material, changes to this Agreement can not be considered. For questions or comments on Agreement terms please contact NCID Technology Development Coordinator.

2. Recipient shall type information in appropriate shaded areas (with especial emphasis on Term #3, the description of the Research Project); print two (2) copies of the agreement; have approved and signed by the authorized **administrative** and **biosafety** officials of the Recipient institution. Both copies must have original signatures.

3. To receive the MATERIAL, Recipient should fax the approved and signed agreement to: 404-638-5476 to the attention of NCID Technology Development Coordinator along with a statement indicating that the signed originals have been placed in the mail with an overnight delivery service to CDC/NCID Technology Coordinator.

4. Recipient should mail or deliver by overnight delivery service the original approved and signed copies to:

   Centers for Disease Control and Prevention
   1600 Clifton Road, N.E., MS A-42
   Attn.: CCID Technology Development Coordinator (TDC)
   Atlanta, Georgia 30333
   Tel 404-639-2620

5. Material will be provided to Recipient upon receipt by the NCID TTC of the faxed signed copy of the Agreement and the statement of mailing. In addition, Recipients from the United States need to provide copy of their current USDA permit, per 9 CFR 122. To obtain such permit, recipient should submit a VS 16-3 application at www.aphis.usda.gov/vs/ncie

6. One fully executed original copy of the Agreement will be returned to Recipient.

PUBLIC HEALTH SERVICE MATERIAL TRANSFER AGREEMENT

This Material Transfer Agreement ("MTA") has been adopted for use by the National Institutes of Health, the Food and Drug Administration and the Centers for Disease Control and Prevention, collectively referred to herein as the Public Health Service ("PHS") in all transfers of research material (Research Material) whether PHS is identified below as its Provider or Recipient.

Provider: Centers for Disease Control and Prevention

Recipient: CSL Limited

1. Provider agrees to transfer to Recipient's Investigator named below the following Original Material (please place an "X" in the box adjacent to the reassortant requested):

   ☐ Influenza A virus reassortant Viet/1203/2004(H5N1)/ PR8-IBCDC-RG

   ☒ Influenza A virus reassortant Anhui/01/2005(H5N1)-PR8-IBCDC-RG6

   ☐ Other Material:

2. THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS. The Research Material will only be used for research purposes by Recipient's investigator in his/her laboratory, for the research project described below, under suitable containment conditions. This Research Material will not be used for commercial purposes such as screening, production or sale, for which a commercialization license may be required. Recipient agrees to comply with all Federal rules and regulations applicable to the Research Project and the handling of the Research Material.

2(a). Are the Research Materials of human origin?

☐ Yes

☒ No

2(b). If Yes in 2(a), were Research Materials collected according to 45 CFR Part 46, "Protection of Human Subjects"?

☐ Yes (Please provide Assurance Number: _____)

☐ No

3. This Research Material will be used by Recipient's investigator solely in connection with the following research project ("Research Project") described with specificity as follows (use an attachment page if necessary):

   The Research Material will be use to generate from progeny virus under GMP conditions seed virus for production of pilot lots of inactivated candidate vaccines for use in human clinical trials.

4. In all oral presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's contribution of this Research Material unless requested otherwise. To the extent permitted by law, Recipient agrees to treat in confidence, for a period of three (3) years from the date of its disclosure, any of Provider's written information about this Research Material that is stamped "CONFIDENTIAL," except for information that

was previously known to Recipient or that is or becomes publicly available or which is disclosed to Recipient without a confidentiality obligation or that the Recipient can establish by reasonable proof is independently developed by employees of the Recipient who had no knowledge of the confidential information disclosed. Any oral disclosures from Provider to Recipient shall be identified as being CONFIDENTIAL by notice delivered to Recipient within ten (10) days after the date of the oral disclosure. Recipient may publish or otherwise publicly disclose the results of the Research Project, but if Provider has given CONFIDENTIAL information to Recipient such public disclosure may be made only after Provider has had thirty (30) days to review the proposed disclosure to determine if it includes any CONFIDENTIAL information, except when a shortened time period under court order or the Freedom of Information Act pertains.

5. This Research Material represents a significant investment on the part of Provider and is considered proprietary to Provider. Recipient's investigator therefore agrees to retain control over this Research Material and further agrees not to transfer the Research Material to other people not under her or his direct supervision without advance written approval of Provider. Provider reserves the right to distribute the Research Material to others and to use it for its own purposes. When the Research Project is completed or three (3) years have elapsed, whichever occurs first, the Research Material will be disposed of as directed by Provider.

6. This Research Material is provided as a service to the research community. IT IS BEING SUPPLIED TO RECIPIENT WITH NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. **PROVIDER MAKES NO REPRESENTATIONS THAT THE USE OF THE RESEARCH MATERIAL WILL NOT INFRINGE ANY PATENT OR PROPRIETARY RIGHTS OF THIRD PARTIES**.

7. When Provider is the PHS: Recipient shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the Research Project. Recipient agrees not to claim, infer, or imply Governmental endorsement of the Research Project, the institution or personnel conducting the Research Project or any resulting product(s). Unless prohibited by law from doing so, recipient agrees to hold the United States Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses and losses arising out of Recipient's use for any purpose of the Research Material.

8. When Recipient is the PHS: The PHS shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the Research Project. The PHS is not authorized to promise rights in advance for inventions developed under this Agreement. Provider acquires no intellectual property rights under this MTA, but may apply for license rights to any patentable invention that might result from this Research Project. It is the intention of PHS that Provider not be liable to PHS for any claims or damages arising from PHS's use of the Research Material; however, no indemnification is provided or intended.

9. The undersigned Provider and Recipient expressly certify and affirm that the contents of any statements made herein are truthful and accurate.

10. This MTA shall be construed in accordance with Federal law as applied by the Federal courts in the District of Columbia.

11. Any additional requirements:

a. **Recipient's Biosafety Official shall accept full responsibility for the safety of the Research Project and that the Research Project will be performed in accordance with applicable institution and Government health and safety regulations and the guidelines detailed in Appendix A[1], as well as *Biosafety in Microbiological and Biomedical Laboratories*, 4th Edition, GPO Stock No. 017-040-00547-4, May 1999, or the most recent revision of these guidelines.**
b. **No later than one month before a publication concerning the results obtained with the Research Material is going to be submitted, Recipient agrees to send a copy or draft of the paper to the Provider's Investigator. If there is no publication, the Recipient agrees to communicate the results of the studies concerning the Research Material to the Provider's Investigator. Any such results shall be kept in confidence in accordance with the Freedom of Information Act (5 U.S.C. ' 552), Department of Health and Human Services regulations (45 C.F.R. ' 5.65), and Executive Order No. 12600.**
c. **In all publications related to the Research Material, its origin and the name given by the Provider must be indicated.**

[1]Appendix A. The Influenza Branch guidelines for the recommended BSL2-enhanced safety procedures for the handling of the Research Material.

NEXT PAGE SIGNATURE PAGE

PUBLIC HEALTH SERVICE MATERIAL TRANSFER AGREEMENT

Certification of Recipient Scientist: **I have read and understood the conditions outlined in this Agreement, and I understand that I must abide by them to receive and use the Research Material.**

RECIPIENT INVESTIGATOR:

Signature:_____ Date:_____

Name: Peter Schoofs
Title: Manager, Influenza Development, R&D

RECIPIENT'S BIOSAFETY OFFICIAL:

Signature: _____ Date: _____
Name of Biosafety Official:
Telephone number:

AUTHORIZED OFFICIAL FOR RECIPIENT:

Signature:_____ Date:_____

Name:
Title:

Signature:_____ Date:_____

Name: Peter Turvey
Title: Company Secretary

Recipient's Mailing Address: CSL Limited
45 Poplar Road
Parkville
Melbourne
Victoria Australia 3052

PROVIDER INVESTIGATOR: Ruben Donis, Ph.D.
Team Leader, Molecular Virology And Vaccines Branch/
Influenza Division/CCID/CDC

AUTHORIZED OFFICIAL FOR PROVIDER:

Signature: _____ Date:_____

Anne Schuchat, MD
Director, National Center for Immunization and Respiratory Diseases

Provider's Mailing Address: Centers for Disease Control and Prevention
CCID Technology Transfer
Mail Stop A-42
1600 Clifton Road, N.E.,
Atlanta, Georgia 30333

PUBLIC HEALTH SERVICE MATERIAL TRANSFER AGREEMENT

APPENDIX A

Influenza Branch/DVRD/NCID Biosafety recommendations for laboratory handling of high growth PR8 reassortants of influenza virus bearing engineered H5 HA derived from highly pathogenic avian influenza virus strains.

Definitions: This appendix concerns the use of vaccine reference stocks of reassortant viruses carrying the internal genes from A/PR/8/34, and the surface genes from highly pathogenic avian influenza (HPAI) strains (e.g., H5N1). The reassortant virus is considered to be equivalent to the H5 low pathogenicity avian influenza (LPAI) viruses with regards to its virulence properties. These reassortants are referred to as DeltaH5-PR8 candidate vaccine reference stocks. Information on risk assessment of these reference vaccine stocks can be obtained at the WHO website URL:
www.who.int/entity/csr/resources/publications/influenza/en/influenzaRMD2003_5.pdf.

Risk assessment: The A/PR/8/34 is considered to be attenuated in humans. The A/PR/8/34 has virulence properties equivalent to LPAI strains. There are no documented human infections with strains of the H5 subtype of LPAI. Therefore, the reassortants are predicted to pose a minimal risk to humans. However, caution is necessary because of the limited experience with vaccine strains possessing a combination of avian genes and genes from a human virus, albeit egg-adapted. While the DeltaH5-PR8 virus is expected to be replication-deficient in humans, there is a remote possibility of secondary reassortment with a normal human influenza A virus which could generate a replication-competent virus.

Laboratory hazards: The primary laboratory hazard is inhalation of DeltaH5-PR8 virus or mucosal exposure from aerosols generated by aspirating, dispensing, mixing, centrifuging or otherwise manipulating virus-infected samples.

Recommended Precautions: Biosafety Level 2 facilities, with enhanced practices and procedures are recommended for research and production activities utilizing live DeltaH5-PR8 candidate vaccine reference stocks.

The enhancements beyond all the applicable BSL2 protocols include:

1) The laboratory where work with DeltaH5-PR8 is performed should have negative pressure relative to the atmosphere and adjacent hallways or laboratories with direct access.

2) All manipulations of open containers with DeltaH5-PR8 candidate vaccine reference stocks should be performed in a class II biological safety cabinet. However this may not be possible in a manufacturing environment and alternative control measures are therefore needed:
    a. use of other suitable barrier systems;
    b. staff should use of powered full-face respirators, equipped with HEPA filters;
    c. antiviral prophylaxis for staff in the production area and those in adjacent areas. Neuraminidase inhibitor antiviral drugs (e.g., oseltamivir, zanamivir) should be available for treatment and post-exposure prophylaxis, as necessary (MMWR May 28, 2004 / 53(RR06);1-40).

3) There should be no need to inactivate effluent from sinks, because any liquid effluent from sinks should have been disinfected by validated procedures and there is little risk of hand-washing effluent posing a hazard to the environment.

4) A code of practice for the work should be prepared, the key features of which are:

   a. Access to the laboratory is restricted to authorized personnel. A sign should be posted at the entrance door during the times that experiments are in progress to indicate this fact. No other experiment of any kind should be conducted simultaneously in the same room where the DeltaH5-PR8 reassortant is being used.
   b. Personnel should wear complete protective gear, including head cover, goggles, N95 nose and face mask, gown, and booties. Double gloves should be used to allow safe disposal of all the protective gear into an autoclave bag within the room.
   c. Showering is not required, as protective clothing and hand washing procedures are normally considered adequate to protect human health and the environment for this level of hazard.
   d. Procedures to prevent exposure of the H5N1 reassortant to normal human and animal influenza viruses. Staff should have received a conventional influenza vaccine to limit their susceptibility to infection with normal human viruses. If pilot lots of DeltaH5-PR8 vaccine are available, staff should receive them.
   e. There should also be an Occupational Health Policy for antiviral prophylaxis or for treatment following accidental exposure to the DeltaH5-PR8 reassortant virus. All personnel at risk should be enrolled in an appropriately constituted respiratory protection program. Personnel should be counseled regarding the risks and monitored for disease symptoms and absenteeism. Personnel should monitor their body temperature daily and report any fever (temperature >38 °C or 100.4 °F) if accompanied by sore throat and cough and/or dyspnea (difficult respiration or laborious breathing).
   f. Review of all working practices to minimize the creation of aerosols from the vaccine virus.
   g. Standard Operating Procedures for the safe decontamination of waste and equipment should be established.
   h. Emergency procedures for events such as spillages documented.
   i. The staff biosafety training program should document the proficiency of the trainees.

5) All virus samples that are not saved for future use in a secure location should be autoclaved immediately and discarded.

6) Storage of baseline serum samples from individuals working with these influenza strains is recommended.

PUBLIC HEALTH SERVICE MATERIAL TRANSFER AGREEMENT

Recipient: CSL Limited

RESEARCH PROJECT
(as needed)