

January 16, 2007

Mr. Dennis Lawyer  
Nuclear Materials Safety Branch  
Region I  
U.S. Nuclear Regulatory Commission  
475 Allendale Road  
King of Prussia, PA 19406-1415

M56  
J-6  
29-00117-06  
03014680

Subject: ADDITIONAL INFORMATION FOR LICENSE AMENDMENT REQUEST:  
CONTROL NUMBER 139603

Dear Mr. Lawyer:

In response to your November 15, 2006 letter, please find below additional information with respect to Merck's October 9 2006 request for "Relief from 10 CFR 33.17(a)(4)".

Following the format suggested in NUREG 1556, Volume 20, "the exemption request must be accompanied by:"

- I. A description of the licensee-proposed exemption and the reason why it is needed;
- II. A description of specific compensatory safety measures that will provide a level of protection equivalent to the regulation for that the licensee-proposed exemption is being requested; and
- III. A discussion of reasonable alternatives that have been considered by the licensee.

**I. Proposed Exemption Description and Why It Is Needed.** The exemption from 10 CFR 33.17(a)(4) would help support research by allowing the licensee to directly transfer radiolabeled compounds for IND Studies to Part 35 Licensees.

Background. Our broad scope license facilitates the creation and development of novel pharmaceutical compounds that are used to treat disease and benefit mankind. These radiolabeled compounds are not radiopharmaceuticals, but are used to gain valuable information about the absorption, distribution, metabolism, and excretion of molecules in the drug research and development process. Such studies are conducted under a Food and Drug Administration's (FDA) Investigational New Drug application (IND) by an investigator at a facility that is licensed by the NRC or Agreement State, typically as Part 35 NRC licensee. This transfer of radioactively-labeled compounds is not a **routine** commercial operation, but is intended to gain additional information concerning the pharmacokinetic performance of these compounds.

Your November 15, 2006 letter suggests that we apply for an exemption from 10 CFR 32.72(a)(2) which would authorize the distribution of materials containing hydrogen-3 or carbon-14 to Part 35 Licensees. This method is not optimal because:

- a. It does not allow the flexibility for studies that could involve radionuclides other than hydrogen-3 or carbon-14. To accommodate future research needs we would appreciate the

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flexibility to transfer authorized materials to allow IND research that could involve microcuries of any licensed radionuclides.

- b. Merck is registered with the FDA as a drug manufacturer, therefore we would not typically qualify for a 10 CFR 32.72 (a)(2) exemption.
- c. We are not a pharmacy, do not make radiopharmaceuticals, or employ pharmacists for these activities.
- d. Implicit in Part 32.72 is commercial distribution of radioactive materials. Infrequent transfer of materials to a Part 35 licensee without financial compensation does not clearly meet the definition of commercial distribution.

**II. Compensatory Safety Measures.** Although we are not requesting an exemption to 10 CFR Part 32.72, we do intend to fully comply with the applicable 10 CFR Part 32.72 requirements as described below:

a. We will satisfy the general requirements specified in 10 CFR 30.33;

b. Most pharmacokinetic studies in support of an IND's will involve microcurie quantities of hydrogen-3 or carbon-14. Radionuclides are chemically bound with compounds that are usually biologically active and typically exist in solid or liquid forms. Containers holding samples are well constructed to prevent leaking of contents during storage, use and transfer. These containers may hold enough radionuclide for multiple doses, but since only small activities are used during the IND trials no special packaging or shielding is needed for transfer of these materials to the Part 35 Licenses.

c. Caution Radioactive Material Labels will be attached to the container holding the radiolabelled compound. The name of the compound and/or radionuclide, the activity present and the date will be written on the label.

d. Merck possesses and uses instrumentation that has the ability to quantify any of the radionuclides that are authorized by our license. This instrumentation will be used to determine the amount of radioactivity in materials that will be transferred to Part 35 Licenses. Furthermore, instrumentation will be tested before use, periodically, and following repair to ensure its accuracy.

### **III. Discussion of Reasonable Alternatives Considered By the Licensee**

While investigating the potential methods for this licensing action, three methods were reviewed.

1. Seeking a Part 32.72 authorization,
2. Seeking a Part 32.72 exemption, and
3. Continuing the request for an exemption to 10 CFR 33.17(a)(4).

As previously discussed the Part 32 authorization or exemption does not fit well for a pharmaceutical licensee who infrequently transfers licensed material to a Part 35 licensee in support of an IND research project.

NRC may have tried to resolve this issue the last time Part 35 was updated. Consider page 5-47 of *NRC's Final Regulatory Analysis 10 CFR Part 20, 32 and 35* (See <http://www.nrc.gov/reading-rm/doc-collections/commission/secys/2000/secy2000-0118/attachment12.pdf>) where it clearly states in a section titled "Benefits" of the new 10 CFR 35.100(d):

"The final rule allows (1) medical use licensees to receive radioactive drugs, for use in RDRC-approved or IND research protocols, prepared and distributed by NRC or Agreement State licensees who are not (Part) 32.72 licensees, and (2) any individual to prepare a radioactive drug in accordance with either an RDRC-approved protocol or an IND protocol."

This document clearly shows that medical use licenses can accept materials from NRC or Agreement State licensees who are not Part 32.72 licenses – but the corollary regulation to authorize broad scope licenses to transfer materials to medical licensees was apparently not addressed.

After much discussion, Merck still requests the exemption to 10 CFR 33.17(a)(4) that would provide the corollary benefit that is associated with 10 CFR 35.100(d). It should be noted that our West Point Pennsylvania License (# 37-01531-07) has maintained this specific exemption, without incident or concerns, for at least the last 16 years.

Your continued work on this amendment request is appreciated. If you have any questions or concerns regarding this matter, please contact our Radiation Safety Officer, Vincent Williams at (732) 594-1434.

Sincerely,



Gregory R. Reinhard, DVM

Cc: Dr. Linda Hostelley                    WP97A-285  
Mr. John J. Miller                        WP44-204  
Mr. Vincent P. Williams                RY80HP