#3

GEN-PROBE
9620 Chesapeake Drive • San Diego, California 92123 • (619) 268-8400

November 21, 1984

U.S. Nuclear Regulatory Commission
Director, Division of Fuel Cycle and Material Staff
Office of Nuclear Material Safety and Safeguards
Washington, DC 20555

Dear Sir:

The following information is submitted in support of being granted a license to distribute exempt quantities of by-product material.

1. Gen-Probe, Inc. has a Specific License (Number 4376-80) to possess Hydrogen-3 (Tritium) as well as other radioactive materials.

2. The appropriate sections (Sections 1, 2, 3, 4, 12, and 13) of NRC Form 313 have been completed. Please reference our Specific License 4376-80 with the State of California for Sections 5-11.

3. The by-product material is to be prepared for distribution in units not exceeding one (1) microcurie each of Hydrogen-3 (Tritium). (See attached sample label). No more than 10 exempt quantities shall be sold or tranferred in any single transaction.

4. The outer package shall be such that the dose rate at the external surface of the package does not exceed 0.5 milli-rem per hour.

5. Each prepackaged unit will bear a durable, legible label (sample label attached):
   a) which identifies the radiosotope and the quantity of radioactivity
   b) which bears the words "Radioactive Material".

6. Each prepackaged unit will have an accompanying brochure (excerpt from that brochure is attached)
   a) which states the contents are exampt from NRC or agreement state licensing requirements.

b) which bears the words "Radioactive Material - Not for Human Use - Introduction into Foods, Beverages, Cosmetics, Drugs, or Medicinals, or into Products Manufactured for Commercial Distribution is Prohibited - Exempt Quantities should not be Combined"
c) which sets forth appropriate additional radiation safety precautions and instructions relating to the handling, use, storage, and disposal of the radioactive material.

7. Our quality assurance procedures for assuring the radioactive content of final containers meet the specifications of the final container label will be as follows:

A) Pre-Fill Testing

The radioactivity of a given volume of the final bulk material will be determined before filling. Three aliquots of the final bulk material will be dispensed into standard counting vials using calibrated pipettes. The radioactivity of each will be measured using liquid scintillation counting instruments described in our California specific license application dated April 3, 1984. Based on the average counts per milliliter of bulk material as determined above and the "maximum fill volume" (see next section) for the product a pre-fill calculation will be done to assure that we will not exceed the radioactivity level as specified on the final product label. If the calculations indicate we would exceed the label limit the bulk will be reworked and the above procedure repeated.

B) Set-Up and In-Process Testing

As part of the filling operation, the filling equipment will be calibrated. Three tared (by weight) containers will be filled and weighed on a calibrated balance. Using the density of the material we will then determine if the equipment has been properly calibrated to dispense the product within the minimum and maximum limits of the fill tolerance of the product. For example, if the volume noted on the product label is 2.0 ml the fill tolerance might be 2.1 ± 0.1 ml, therefore the "maximum fill volume" would be 2.2 ml (as used in Section A) for the product. Every 1,000 containers or 30 minutes, whichever comes first, and after completion of the fill, the calibration of the filling equipment will be re-verified using the above procedure. If at any time it is determined that the filling equipment is out of tolerance (for example, less than 2.0 ml or greater

than 2.2 ml in the above sample), it will be recalibrated and retested. all materials dispensed (if any) between the approved and unapproved calibration check would be reworked.

C. Final Testing

The appropriate number of filled containers (minimum of three per lot) will be randomly selected and aliquots placed into the counting vials by using calibrated pipettes. The same procedure will then be used as described in section A (Pre-Fill Testing) to verify that we will not exceed the radioactivity level as specified on the final product label. If the calculation indicates we would exceed the label limit the lot will be reworked.

8. Final Container Wipe Test

Wipe test the appropriate number of final containers (minimum of 3) with Whatman Filter Paper DE81, 2.4 cm. Place each respective filter into a scintillation vial and add 10 ml of scintillation solution (Cytoscint, Westchem). Count vials in liquid scintillation counter (calibrated). Determine average counts; if average counts are greater than 200 cpm per container the lot of containers must be surface decontaminated.

After decontamination retest containers and determine if average is less than 200 cpm for each container.

9. The radioactive material to be distributed will be part of in-vitro test kits for research and/or diagnostic use. Kits which will be intended for diagnostic use will be manufactured in accordance with Section 26685 of the Sherman Food, Drug and Cosmetic Law (Division 21 of the California Health and Safety Code).

If you should find that additional information is required to complete this application please contact me as soon as possible. The phone number at Gen-Probe is (619) 268-8400.

Thank you for your help and cooperation in processing our request.

Sincerely,

David E. McCarty
Vice President - Operations

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Sample Brochure

Warnings and Precaution

1. FOR IN-VITRO RESEARCH ONLY

2. THIS RADIOACTIVE MATERIAL IS EXEMPT FROM NRC OR AGREEMENT STATE LICENSING REQUIREMENTS

3. RADIOACTIVE MATERIAL - NOT FOR HUMAN USE - INTRODUCTION INTO FOODS, BEVERAGES, COSMETICS, DRUGS, OR MEDICINALS, OR INTO PRODUCTS MANUFACTURED FOR COMMERCIAL DISTRIBUTION IS PROHIBITED - EXEMPT QUANTITIES SHOULD NOT BE COMBINED"

   a) Store radioactive materials in the original container in a specially designated area. Locate this storage area as far from the work area as practical.
   b) Do not pipette radioactive material by mouth.
   c) Use radioactive material only in designated work areas with absorbent covering on the laboratory bench surfaces.
   d) Wipe up any spills with an absorbent material, and wash the involved surface with a suitable detergent. Dispose of contaminated material properly.
   e) Dispose of unused radioactive material from this kit by placing in a sink and flushing with a large quantity of water.
   f) Do not eat, drink or smoke in designated work areas.
   g) Wear disposable gloves, laboratory coats, and other appropriate protective devices when handling radioactive materials.
   h) Do not permit persons under 18 years of age to handle radioactive material or enter radioactive areas.

USERS OF THIS KIT SHOULD ADHERE TO THESE PRECAUTIONS OR SIMILAR LOCAL PRECAUTIONS WHICH HAVE BEEN ESTABLISHED WITH CONSISTENCY TO U.S. NUCLEAR REGULATORY COMMISSION REQUIREMENTS.

SAMPLE LABEL

GEN-PROBE

REAGENT

MYCOPLASMA
Probe Solution

2.0 ml

Containing ^{3}H Mycoplasma
DNA probe

Store at Room Temperature

For Research Use Only

Lot:

Exp:

Not for Internal or External
Use in Humans or Animals

Patent Pending

Gen-Probe
San Diego, CA 92123