MAY 30 1985

License No. --
Docket No. 030-21252
Control No. 03754

Cadema Medical Products, Inc.
ATTN: Maurice E. Bordoni
President
569 North Street
P. O. Box 250
Middletown, New York 10940

Gentlemen:

This is in reference to your application dated April 15, 1985, for a reagent kit distribution authorization. In order to continue our review, we need the following additional information:

1. Please provide a letter from the F.D.A. that states that NDA 19-180 is approved. The March 14, 1984 letter in Section 10.2.1 of your NRC application indicates only that application for your Antimmy Trisulfide Colloid Kit has been received. This letter does not signify NDA approval of the kit by the F.D.A. Alternatively submit a copy of the letter from F.D.A. with the IND approval for studies with this kit.

2. Please provide a letter from the F.D.A. acknowledging your use of Brookhaven National Labs, IND No. 12003 for Red Blood Cell Labeling Kit and that you may proceed with your proposed study.

3. Please submit pages 2, 3, 4, and 5 of the October 15, 1984, letter from the F.D.A. regarding your Pentatate Sodium kit. Please clarify whether you have N.D.A. approval from the F.D.A. for renal scanning and function studies or is the use of this kit still under IND 24,406 until you have completed the studies for the total submittal to the F.D.A.

4. Please clarify whether you have satisfied the F.D.A.'s indication of chemistry deficiencies with your Mini-Microaggregated Albumin Colloid Reagent kit as stated in the May 11, 1984 letter and whether the F.D.A. has removed your restriction to only 40 patient studies.

5. The NRC's Draft Regulatory Guide for Distribution to Group Medical Licensees, Task FC 406-4 (February, 1985) states in Section 10.3.4 that after radiopharmaceuticals have been prepared using the reagent kit, they must be in containers labelled in compliance with 10 CFR 20.203 and 10 CFR 32.73(a)(4). Please submit an actual color sample of the label to be placed on the vial and the shielded lead container surrounding the vial for each of the four kits you wish the NRC to license.

   Under 10 CFR 20.203(f), the NRC licensee who reconstitutes a reagent kit is required to label the kit reaction vial. A label that is placed on the lead shield surrounding the vial does not fulfill this requirement if the vial can become separated from the shield.

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In addition to the labels that the manufacturer supplies for the lead shield that surrounds the reaction vial, we believe that the manufacturer should supply labels, and directions to complete and affix them, that are adequate to fulfill the requirements of 10 CFR 20.203(f). After reconstitution, the vial labeling must include a radiation caution symbol of the design and colors specified in Section 20.203 (magenta or purple on a yellow background), the words "CAUTION, RADIOACTIVE MATERIAL", and identification of the radioactive contents. These vial labels may need to be quite small in size so as not to obliterate F.D.A.-required labeling; but, as a minimum, they should include the radiation caution symbol, the words "CAUTION, RADIOACTIVE MATERIAL", the isotope, and space to indicate the date of reconstitution.

As an alternative, some kit manufacturers have solved this problem by providing a single label which attaches to the neck of the reaction vial by a string and therefore extends out over the lead shield. In addition, we will consider any other solution that you may propose.

6. Section 10.3.4 of the NRC's Draft Guide, Task 406-4 (February, 1985) states that the licensing statement required by 10 CFR 32.73(a)(ii) must be contained on a label, leaflet or brochure accompanying the reagent kit. Further radiation safety instructions must be included with the procedures for processing the kit. These radiation safety instructions as a minimum should specify:

   A. The use of waterproof gloves,
   B. The use of shielded syringe to introduce the radioactive material,
   C. The use of an adequate (e.g., lead or leaded glass) vial shield with an appropriate (e.g., lead) fitted cover,
   D. Completing and affixing a label identifying the radionuclide, chemical and physical form, activity, and assay time and date,
   E. The use of adequate shielding (e.g., shielded syringe) for withdrawing and administering patient doses, and
   F. The assay of patient doses before administration.

   Specifically we note:

   a. The outer box label and package insert for your Antimony Sulfur Colloid Kit does not contain

      1. the 10 CFR 32.73(a)(5)(ii) licensing statement and
      2. the instructions specified in A., B., C., and E., above.

      Additionally, your direction #2 on the preparation does not include placement of the reaction vial in a vial shield with appropriate fitted cover prior to adding the technetium .

   b. The package insert preparation instructions for the BNL Red Blood Cell kit does not contain:

1. the 10 CFR 32.73(a)(iii) licensing statement and
2. the instructions specified in A., B., D., and E. above.

Additionally, your direction for dose calibrator measurement does not state that this should be performed prior to administration of the product.

c. The package insert preparation instructions for the Pentetate Kit (DTPA) does not contain:

1. the 10 CFR 32.73(a)(5)(iii) licensing statement and
2. the instructions specified in A., B., D., E., and F. above.

Additionally, although you state "Place the vial in a suitable radiation shield suitably labeled and identified", you do not include the fitted (leaded) cover nor specify what label should be affixed to the vial and vial shield.

d. The package insert preparation instructions for the Albumin Colloid Kit does not contain:

1. the 10 CFR 32.73(a)(5)(ii) licensing statement and
2. the instructions specified in B., D., E., and F.

Additionally, although you state "Place the vial in a suitable radiation shield suitably labeled and identified", you do not include the fitted (leaded) cover nor specify what label should be affixed to the vial and vial shield.

Your preparation procedures for these four kits should be modified to include instructions substantially similar to the following:

1. Complete and affix the radiation warning label to the reaction vial.

2. Use waterproof gloves during the preparation procedure.

3. Place the reaction vial in a suitable lead shield that has a fitted lead cap.

4. Use a shielded syringe when introducing the pertechnetate solution into the reaction vial.

5. Place the lead cap on the vial shield prior to mixing the contents by swirling, inversion, etc.

6. Maintain adequate shielding during the life of the product by using the lead vial shield with lead cap in place and by using a syringe shield for withdrawing and injecting the preparation.

7. Complete and affix the "radioactive contents" label to the vial shield.

8. Assay patient dose prior to administration.

We recognize that the changes requested in this letter may have to be coordinated with other agencies, sub-contractors, etc. In addition, you may wish to use up existing stocks of package inserts. If so, please submit drafts of the changes that you will make and indicate the anticipated future date that these changes can be incorporated into each package insert.

We will continue our review upon receipt of this information. Please reply in duplicate to my attention at the Region I office and refer to Mail Control No. 03754.

Sincerely,

Original Signed By:
John E. Glenn

Jenny M. Johansen, M.S.
Nuclear Materials Safety Section B
Division of Radiation Safety
and Safeguards

Enclosures:
1. 10 CFR Part 32
2. Regulatory Guide: Draft Guide Distribution Group Medical Licensees, Task FC 406-4 (February, 1985)

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