August 16, 1983

Mr. Vandy Miller, Branch Chief
Material Licensing Branch
Division of Fuel Cycle & Material Safety
Office of Nuclear Material Supply & Safeguards
U S Nuclear Regulatory Commission
Washington, DC 20555

Dear Mr. Miller:

The American Pharmaceutical Association is responding to a draft guide for the preparation of applications for nuclear pharmacy licenses. I regret that a change in Association staff caused a delay in transmitting these comments. I trust, however, that they will be of use to you and your staff in finalizing the draft.

The draft guide was referred to the Association's Academy of Pharmacy Practice Section on Nuclear Pharmacy and the following represents a consensus of the Section's Committee on Regulatory Affairs.

1. Section 1, 1.1 Purpose of Guide. It is felt that clarification is necessary with respect to the term "distribution." It is an inappropriate term if the purpose of this guide is to provide assistance in the preparation of applications for NRC licensure of nuclear pharmacies licensed by states for the practice of pharmacy. We believe the correct term to be used is "dispensing," for there is no true distribution function in the practice of pharmacy.

2. Section 3, page 3, paragraph 3, Cautionary Statement. Nuclear pharmacists feel that incorporation by reference of referred to sections of this or other regulatory guides into the terms and conditions of a license is appropriate. However, we would suggest that referencing should be to a dated regulatory guide. Thus, if the guidelines change, NRC would have the obligation to notify licensees of any changes or allow the conditions of the originally referenced guideline(s) to stand. In this way, NRC could be assured that licensees are aware of recent regulatory change and that required operational revisions can be instituted in a timely fashion.

3. Section 3, page 4, paragraph 3, "deficiency correspondence." This term has a negative connotation. Such correspondence is really "educational" to inform applicants where they have failed to stay abreast of minimal criteria for licensure. It is suggested that the last sentence of this paragraph read as follows:

   Such submissions require a customized review and may cause delay in the issuance of the license.
4. **Section 4, Item 3: Authorized Users.** The two paragraphs included are satisfactory as written. However, it is suggested that the following be added to this item.

The duties and responsibilities of an authorized user in charge of facility operations include:

c. Maintaining an inventory of all radionuclides on hand at the facility.

This suggestion is made because these duties and responsibilities can be most effectively performed by an authorized user who, by license requirement, must be physically present whenever licensed material is being used. This transfer of responsibility would assure direct supervision of the indicated activities on a 24-hour basis. In addition, it would alleviate the redundancies created as a result of combining duties which require the physical presence of an individual at specific times during the use of licensed material with those duties that do not require the presence of an individual at a specific time. It is doubtful that NRC would desire licensed facilities to have more than one individual in charge of the remaining duties and responsibilities described under Item 4. Thus, this arrangement would remove the severe limitations imposed as a result of requirements to have a single individual present on a day-to-day basis. This change would allow for a radiation safety officer vacation, sickness, etc. and make it possible for this individual to have a more flexible schedule and yet fulfill the duties and responsibilities of a radiation safety officer.

5. **Section 4, Item 4: Radiation Safety Officer.** The duties and responsibilities of the radiation safety officer should include the following activities:

a-d. of this item as written.
g-h. of this item as written.
i. Coordinating and monitoring the radioactive waste disposal program.
j. Monitoring the safe storage of all radioactive materials not in current use.
k. of this item as written.
l. Monitoring the quantities of radionuclides at the facility to ensure that the amounts are authorized by the license.

Statements e. and f. should be deleted and transferred to Section 4, Item 3, as noted previously. The term "radiopharmacy" should be deleted and replaced with the term "nuclear pharmacy" in the last paragraph.

6. **Section 4, Item 6: Site Description.** We suggest that the description of acceptable locations for nuclear pharmacies make allowance for the possibility that a centralized nuclear pharmacy may be located in a hospital. With respect to license criteria f., it is felt that NRC should clarify the extent to which a nuclear pharmacy must instruct the local fire department in appropriate emergency procedures.
7. Section 4, Item 7: Facility Description. In paragraph 4 under licensing criteria, the last sentence should indicate that "unqualified" delivery persons should not be given access to areas where licensed material is stored. Inclusion of the word "unqualified" will differentiate between employees of the facility who are qualified and commercial delivery persons not associated with the facility.

8. Section 4, Item 8: Personnel Monitoring Procedures. With respect to statement d., to require participation in a voluntary program appears to be an anomaly.

9. Section 4, Item 10: Procedures for Calibration of Survey Instruments. It is proposed that statement f. be reworded in the following manner: ..., be maintained for at least 2 years following the calibration, or to the first NRC inspection following calibration.

10. Section 4, Item 11: Procedures for Calibration of Dose Calibrators. It is proposed that the word "all" in licensing criteria a., statement 3, be replaced by the word "several." It is felt that the constancy of operation of a dose calibrator can be ascertained after checking several commonly used radionuclide settings. With respect to statement 2 of licensing criteria d., it is noted that the use of serial dilutions for linearity checks would not be consistent with the ALARA philosophy. Thus the term "serial dilutions" should be deleted and replaced with the term "serial shielding." This change should also be reflected in the note at the bottom of page 15. Lastly, it is suggested that licensing criteria e. be reworded to state that the records be maintained for a period of 2 years from previous NRC inspection. This would allow licensees to purge records after inspection, and maintain them for a maximum of two years.

11. Section 4, Item 12: Personnel Training Program. It is suggested that a licensing criteria d. be added to state that delivery personnel be specifically instructed as to methods for storing licensed materials during transport, upon delivery during work hours and when making deliveries prior to or after work hours.

12. Section 4, Item 13: Procedures for Receipt of Shipments Containing Radioactive Materials. It is suggested that licensing criteria b. be changed to read as follows:

   b. That these written directions identify the area where deliveries are to be presented during working hours and left during hours the facility is closed. All delivery personnel shall have an authorized user or his designee inspect and sign for all radioactive shipments delivered during working hours.

13. Section 4, Item 15: General Procedures for Safe Use of Radioactive Materials. It is suggested that the word "lead" be deleted from license criteria d.. Not all shields are necessarily lead; in fact a lead syringe shield for a beta-emitter would not be appropriate. Materials such as tungsten, leaded glass, etc. may also be suitable for construction of shielding. It is suggested that license criteria g. be reworded as follows:
g. That every vial, syringe and capsule containing greater
than 10 microcuries of gamma-emitting radiopharmaceuticals
for imaging purposes be assayed in a dose calibrator prior
to dispensing for use in humans.

We question the accuracy and necessity for the assay of "every" gamma-emitting
radiopharmaceutical dose less than 10 microcuries. Many times it is impossible
to obtain meaningful dose calibrator assay data when Group I radiopharmaceuticals
are used for diagnostic uptake, dilution and excretion type studies. For example,
is it meaningful to assay Cyanocobalamin Co 57 Capsules in a dose calibrator?
It should be sufficient in these cases to accept the manufacturer's calibration
and labeling information for verification of dosage. This practice would be no
different than a pharmacist dispensing any final dosage form of a prescription
drug in the normal course of the practice of pharmacy. Lastly, the term "distribution"
 is not appropriate in that pharmacists do not distribute prescription
drugs or radiopharmaceuticals. They dispense these items to physicians and
patients for their use.

14. Section 4, Item 17: Area Survey Procedures. An inconsistency exists with
respect to the required detection sensitivity detailed in license criteria f.
vs. that identified in Appendix I, statement 4b. It is thought that a detec-
tion sensitivity of 220 dpm per 100 square centimeters is correct. License
criteria i. creates the need for a more general statement regarding maintaining
records for NRC inspection. It is felt that all periods of record maintenance
should be uniform (e.g., 2 years) for simplicity and to prevent errors.

15. Section 4, Item 19: Retrieval of Waste from Customers. It is suggested that
the phrase "are contaminated with" in license criteria a. be deleted and
replaced with the word "contain." Items can contain radiopharmaceuticals and
not be contaminated with them. The term contamination is a negative term in
our estimation.

16. Section 4, Item 20: Special Procedures and Precautions for Operations That
Involve Opening and Dispensing Miccurie Quantities of Liquid Iodine. It is
suggested that the term "well below" in the first sentence of license criteria
b. be deleted and the term "within or below" be inserted. The term well below
indicates that 10 CFR 20.106 is an inadequate regulation. We do not feel this
is true.

17. Section 4, Item 22: Distribution Procedures. An item of this title is totally
inappropriate for inclusion in this guide. The item as written represents a
classic example of NRC's misunderstanding of the nature of pharmacy practice
and how NRC regulatory responsibilities relate to the activities of pharmacists.
NRC consistently fails to recognize that pharmacies, including nuclear pharmacies,
do not "distribute" drugs when functioning in the capacity of a licensed pharmacy.
A facility with a pharmacy license can, however, be a manufacturer and distrib-
utor of drugs if registered as such with FDA. Thus, a single facility may
participate in both activities but not at the same time. We feel this guide
should pertain to the operation of a facility as a pharmacy and not as a
manufacturer or distributor of drugs. Therefore, there would be no need to
address "distribution procedures" in a guide for the preparation of applications for nuclear pharmacy licenses. Discussions of "distribution procedures" are appropriate only in guides and regulations which pertain to manufacturing and distribution. Thus, we suggest the title of this item be changed to "Dispensing Procedures." The first paragraph of the suggested item can be the same as that written in the current item under licensing criteria. The following statement should be added:

The applicant provides assurance that the nuclear pharmacy will dispense radiopharmaceuticals on a prescription basis in accordance with all applicable laws and regulations governing the practice of pharmacy.

All other statements should be deleted. Any further statements by NRC regarding "dispensing" are totally inappropriate. The NRC is erroneous in its interpretation of FDA's position on exemptions for pharmacy and should not be allowed to make their errors guidelines. The FDA does not limit physician prescriptions to IND/NDA radiopharmaceuticals nor does it limit pharmacy practice to repackaging IND/NDA radiopharmaceuticals (see Am. Pharm. NS 20, No. 8, Aug. 1980/444). These FDA interpretations must be challenged and deleted.

18. Section 4, Item 23: Product Labels. The term "distributed" in the statement boxed at the bottom of page 29 of this item should be changed to "dispensed" for the reasons specified previously.

19. Section 4, Item 24: Product Shielding. The sentence under licensing criteria should end after the term "community hospitals." The phrase "where qualified radiation safety experts may not be available" has a negative connotation. We feel it is not necessary to explain the need for adequate shielding as this need would be obvious to nuclear pharmacists.

20. Section 4, Item 25: Procedures for Packaging and Transporting Radiopharmaceuticals. It is suggested that the requirement for submission of step-by-step procedures for packaging and transporting radiopharmaceuticals to customers be deleted. A statement by the applicant indicating that all applicable D.O.T. regulations will be complied with should be sufficient. It is felt that this does not represent one of the few critical areas where written step-by-step procedures are required.

21. Section 4, Item 26: Independent Audit Program. The item as written requires clarification with respect to acceptable relationships which may exist between the nuclear pharmacy and the individual or group that will ensure regulatory compliance. We also request that NRC issue further statements as necessary to clarify the intent of guidelines for independent audit programs. Lastly, the frequency of independent audits should be specified.

22. Appendix A, Acceptable Training and Experience for Authorized User and Radiation Safety Officer. Regarding the paragraph (pg. 38) to be inserted at the end of Part A, we feel that the term "formal training course" needs clarification. By what mechanism does a course become "formal"? Does formal mean...
"certified"? If so, by whom? Clarification is also necessary regarding the term "qualified instructor" under Part B. It is felt that a qualified instructor must be an authorized user. In addition, experience in handling unsealed radioactive material should be obtained under direct supervision. The requirement to test the eluate of Technetium Tc 99m generator systems for alumina contamination in statement 6, Part B, should be deleted. The testing for alumina contamination is not required by FDA and does not relate to occupational or environmental radiation safety. With respect to figures 1 and 2, we feel clarification is necessary in order to differentiate the information required for documentation of training vs. experience. As an example, consider the case of an applicant receiving training in a laboratory session where the applicant actually performs the activities outlined under figure 2. Assume, further, he does so under the direct supervision of a qualified instructor who is an authorized user. Does this time count as training, training and experience, or experience in handling unsealed radioactive material?

Most importantly, we would like to suggest the following statement be added to this appendix as Part C:

C: Alternative: Certification by the Board of Pharmaceutical Specialties (BPS) in nuclear pharmacy will be accepted as evidence that a pharmacist has had adequate training and experience to possess and dispense Group I, II, III, IV and V radiopharmaceuticals.

In support of this suggested alternative, the BPS intends to initiate acceptance dialogue with NRC. The BPS will send the Commission evidence of eligibility requirements, accreditation programs, and examination procedures which assure that NRC's criteria will be met. We request that these submissions be examined, when presented, by the appropriate NRC staff.

23. Appendix B, Byproduct Material to be Possessed and Used. There is no sample nuclear pharmacy license suggesting the format to submit information regarding the byproduct material to be possessed and used in this appendix.

24. Appendix C, Acceptable Procedures for Calibration of Dose Calibrator. We question the use of significant figures when listing correction factors in step 3 of the test for instrument linearity. With respect to the test for instrument accuracy, we feel the specifications for the container of a low energy standard (Cobalt Co 57) should indicate that the container must be of the same thickness and material as the containers of actual samples to be measured. We feel this change is necessary as samples for assay will be in plastic syringes in a majority of cases. However, it is possible that some licensees would perform assays of byproduct material in glass. Thus, this change would require use of the most appropriate standard container materials.

25. Appendix F, Acceptable Procedures for Safety Opening Packages Containing Radioactive Material. With respect to statement f. of this appendix it is noted that applicable regulations, regarding wipe testing of external surfaces
of final source container shields, do not specifically require testing of every container as implied here. We feel it is necessary that NRC make statements as necessary to clarify their intent to require this test on every final source container shield.

26. Appendix G, Acceptable General Rules for Safe Use of Radioactive Material. It is requested that NRC clarify the meaning of the term "radiation level" in statement 12 of this appendix.

27. Section 4, Contents of an Application. We request that NRC indicate if a nuclear pharmacy license application should be submitted on a specific NRC form. Also, clarification is necessary with respect to the number of application copies required when submitting the original. Several applicants have indicated that confusion exists and that it is a potential source for the delay in the issuance of licenses.

In general, the nuclear pharmacists' responses have been quite positive. There is a definite need for this type of guide and APhA commends NRC for its initiative in developing the guide.

These comments summarize the responses of the Section on Nuclear Pharmacy, Regulatory Affairs Committee and those received from other concerned nuclear pharmacists.

Sincerely,

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Director of Professional Affairs

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