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Chapter I - Atomic Energy Commission

PART 30 - LICENSING OF BYPRODUCT MATERIAL

General License for Diagnostic Uses of Certain Byproduct Materials

On June 6, 1964, the Commission published in the Federal Register (29 F. R. 7393) a proposed amendment of its regulation, "Licensing of Byproduct Material", 10 CFR 30, which would generally license specified quantities and forms of iodine 131, cobalt 58, cobalt 60, and chromium 51 for use by physicians for diagnostic purposes.

In reference to the proposed amendment the Commission has received numerous comments from licensees, medical societies, and other interested persons. The majority of comments were favorable to the proposed amendment although a number of the letters received by the Commission opposed the amendment. Several specific comments suggested that the scope of the general license be broadened or that certain limitations of the general license be liberalized. It was suggested, for example, that the proposed possession limits for the generally licensed byproduct materials be increased and that iodinated fats and fatty acids for gastro-intestinal function studies be added to the general license.

The Commission has given careful consideration to all comments received and has concluded that the proposed general license should be published as an effective rule substantially in the form published on June 6, 1964. There is one difference, however, in the amendment set forth below from the proposed rule published on June 6, 1964. Iodine 125 as iodinated human

serum albumin (IHSA) has been added to the general license for determinations of blood and blood plasma volume. A physician is authorized to possess at any one time under the general license not more than 200 microcuries of iodine 125.

A statement of radiation safety considerations for iodine 131, cobalt 58, cobalt 60, and chromium 51 was included in the Notice of Proposed Rule Making published on June 6, 1964. The following is a statement of radiation safety considerations for iodine 125.

Statement of Radiation Safety Considerations for Iodine 125

Iodine 125, as iodinated human serum albumin, is currently produced and distributed under a product license issued by the Secretary, Department of Health, Education and Welfare. IHSA-I-125 has a useful shelf-life substantially greater than the equivalent product IHSA-I-131.

Iodine 125 has a considerably longer physical half-life (60 days) than I-131 (8 days), but the energy liberated per disintegration is about a factor of 10 less for I-125 than for I-131. In general, the latter consideration tends to make I-125 a less significant source of radiation exposure than I-131, per unit of activity.

From the point of view of external exposure, the dose rate near a given source will be about a factor of 2 less for I-125 than for I-131. More importantly, however, the radiation energies emitted by I-125 are such that it is considerably easier to shield, and under comparable handling conditions, including spills, I-125 would be expected to result in considerably lower external exposures.

Comparable internal radiation dose to the thyroid would be expected from I-125 as from I-131 for a given amount of activity

in the form of iodide. In other forms, the I-125 would be expected to result in notably less exposure per unit of activity administered than I-131, since the biological half-lives in the body are controlling and these are independent of the isotope involved.

A major advantage of the use of I-125 over I-131 is that, with appropriate instrumentation, sensivity can be improved, leading to possible reductions in the amount of activity required for a given medical test. Hence, it is likely that there will be some reduction in future patient exposures for a given medical test resulting from the use of I-125 as opposed to I-131.

In conclusion, there is reason to believe that I-125 may be expected in the future to result in some reduction in exposure. With proper storage, IHSA-I-125 has a longer useful shelf-life than IHSA-I-131.

Except for the addition of IHSA-I-125 to the general license, the text of the amendment is the same as the proposed general license published on June 6, 1964. The physician is required to register with the Commission prior to receiving byproduct material under the general license. The general license expressly limits use of the specified materials as to chemical form of the byproduct material, the drug which is labeled by the radioactive material, and the authorized use of the radiopharmaceutical. For example, there are only two authorized uses under the general license for iodine 131: (a) iodine 131 as iodinated human serum albumin (IHSA) for determinations of blood and blood plasma volume; and (b) iodine 131 as sodium iodide for measurement of thyroid uptake. The authorized use of iodine 125

as iodinated human serum albumin is for determinations of blood and blood plasma volume.

The authorized use of cobalt 58 or cobalt 60 under the general license is for the measurement of intestinal absorption of cyanocobalamin. The authorized use for chromium 51 as sodium radiochromate is for determination of red blood cell volumes and studies of red blood cell survival time.

The limitations set forth in the earlier proposal are retained in this amendment. These include possession limits and limitations on storage and transfer of the radiopharmaceutical. The radiopharmaceutical must be in the form of capsules, disposable syringes or other forms of prepackaged individual doses.

Radiopharmaceuticals used under the general license may not be administered to a woman known to be pregnant or to a person under 18 years of age. The general licensee is exempt from the requirements of 10 CFR 20 with respect to the byproduct materials covered by the general license.

The radiopharmaceutical manufacturer is required to obtain a specific license authorizing distribution of radiopharmaceuticals for use under the general license. The manufacturer must submit evidence that the radiopharmaceutical is to be manufactured, labeled, and packaged under a new drug application approved by the Food and Drug Administration or a license for a biologic product issued by the Department of Health, Education and Welfare.

The Atomic Energy Commission will work with the Food and Drug Administration and the Department of Health, Education and Welfare on their labeling requirements for the generally licensed radiopharmaceuticals and the radiation safety information to be included in the brochures which accompany the generally licensed radiopharmaceuticals.

During the first few years the general license is in effect the Commission will conduct a study to evaluate the effects of the general license. Upon the basis of this experience the Commission will reevaluate the general license and determine whether it should be continued, withdrawn, or expanded to include additional materials and uses.

In view of the limited scope of the general license, the low levels of radiation involved, the manner in which diagnostic radioisotopes are used, and the fact that no processing of the radiopharmaceutical by the physician would be required, the Commission considers that no significant question of radiation safety is presented by the proposed general license.

It is recognized that only limited diagnostic programs are possible under the general license. The specified possession limits are relatively low and only a few forms of radiopharmaceuticals and authorized uses are included. A specific license will be required for those physicians who need a higher possession level, wish to employ other radiopharmaceuticals, or propose to use the specified radiopharmaceuticals for purposes other than those authorized under the general license.

Pursuant to the Atomic Energy Act of 1954, as amended, and the Administrative Procedure Act of 1946, the following amendment of Title 10, Chapter I, Part 30, "Licensing of Byproduct Material," is published as a document subject to codification to be effective thirty (30) days after publication in the FEDERAL REGISTER.

1. A new §30.29 is added to read as follows:

"30.29 General license for medical use of certain quantities of byproduct material.

(a) A general license is hereby issued to any physician to receive, possess, transfer, or use for any of the

following stated diagnostic uses, in accordance with the provisions of paragraphs (b), (c), and (d) of this section, the following byproduct materials in capsules, disposable syringes or other forms of prepackaged individual doses;

(1) Iodine 131 as sodium iodide (NaI^{131}) for measurement of thyroid uptake;

(2) Iodine 131 as iodinated human serum albumin (IHSA) for determinations of blood and blood plasma volume;

(3) Iodine 125 as iodinated human serum albumin (IHSA) for determinations of blood and blood plasma volume;

(4) Cobalt 58 for the measurement of intestinal absorption of cyanocobalamin;

(5) Cobalt 60 for the measurement of intestinal absorption of cyanocobalamin;

(6) Chromium 51 as sodium radiochromate for determination of red blood cell volumes and studies of red blood cell survival time.

NOTE: Paragraph 30.24(k) of this part requires manufacturers of radiopharmaceuticals which are under the general license in this paragraph to include the following statement in the label affixed to the container or in the leaflet or brochure which accompanies the radiopharmaceutical:

"This radioactive drug may be received, possessed, and used only by physicians licensed to dispense drugs in the practice of medicine. Its receipt, possession, use and transfer are subject to the regulations and a general license of the United States Atomic Energy Commission or of a State with which the Commission has entered into an agreement for the exercise of regulatory authority.

(Name of Manufacturer) "

(b) No physician shall receive, possess, use, or transfer byproduct material pursuant to the general license established by paragraph (a) of this section until he has filed

Form AEC-482, "Registration Certificate - Medical Use of Byproduct Material Under General License" with the Director, Division of Materials Licensing, United States Atomic Energy Commission, Washington 25, D.C. 20545, and received from the Commission a validated copy of the Form AEC-482 with registration number assigned. The registrant shall furnish on Form AEC-482 the following information and such other information as may be required by that form:

(1) Name and address of the registrant;

(2) A statement that the registrant is a duly licensed physician authorized to dispense drugs in the practice of medicine, and specifying the license number and the State in which such license is valid; and

(3) A statement that the registrant has appropriate radiation measuring instruments to carry out the diagnostic procedures for which he proposes to use byproduct material under the general license of 10 CFR 30.29 and that he is competent in the use of such instruments.

(c) A physician who receives, possesses or uses a pharmaceutical containing byproduct material pursuant to the general license established by paragraph (a) of this section shall comply with the following:

(1) He shall not possess at any one time, pursuant to the general license in paragraph (a) of this section, more than:

(i) 200 microcuries of iodine 131,

(ii) 200 microcuries of iodine 125,

(iii) 5 microcuries of cobalt 58,

(iv) 5 microcuries of cobalt 60, and

(v) 200 microcuries of chromium 51.

(2) He shall store the pharmaceutical until administered in the original shipping container or a container providing equivalent radiation protection;

(3) He shall use the pharmaceutical only for the uses authorized by paragraph (a) of this section;

(4) He shall not administer the pharmaceutical to a woman with confirmed pregnancy or to a person under 18 years of age;

(5) He shall not transfer the byproduct material to a person who is not authorized to receive it pursuant to a license issued by the Commission or an agreement State, or in any manner other than in the unopened, labeled shipping container as received from the supplier, except by administering it to a patient.

(d) The registrant possessing or using byproduct material under the general license of paragraph (a) shall report in duplicate to the Director, Division of Materials Licensing, any changes in the information furnished by him in the "Registration Certificate - Medical Use of Byproduct Material Under General License," Form AEC-482. The report shall be submitted within 30 days after the effective date of such change.

(e) Any person using byproduct material pursuant to the general license of paragraph (a) of this section is exempt from the requirements of Part 20 of this chapter with respect to the byproduct materials covered by the general license."

§30.24 (Amendment)

2. A new paragraph (k) is added to §30.24 to read as follows:

"(k) Manufacture and distribution of byproduct materials for medical use under general license.

An application for a specific license to distribute byproduct material for use by physicians under the general license of § 30.29 will be approved if:

(1) the applicant satisfies the general requirements specified in § 30.23;

(2) the applicant submits evidence that the byproduct material is to be manufactured, labeled, and packaged in accordance with a new drug application which the Commissioner of Food and Drugs, Food and Drug Administration, has approved, or in accordance with a license for a biologic product issued by the Secretary, Department of Health, Education and Welfare;

(3) the following statement, or a substantially similar statement which contains the information called for in the following statement, appears on the label affixed to the container or appears in the leaflet or brochure which accompanies the package:

'This radioactive drug may be received, possessed and used only by physicians licensed to dispense drugs in the practice of medicine. Its receipt, possession, use and transfer are subject to the regulations and a general license of the United States Atomic Energy Commission or of a State with which the Commission has entered into an agreement for the exercise of regulatory authority.

(Name of Manufacturer)'"

Authority: Sec. 161, 68 Stat. 948; 42 U.S.C. 2201.

Dated at Washington, D. C., this 30th day of April, 1965.

FOR THE ATOMIC ENERGY COMMISSION

W. B. McCool
Secretary