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Regulatory Guide

BIOASSAY REQUIREMENTS FOR ^{125}I AND ^{131}I IN MEDICAL, TEACHING AND RESEARCH INSTITUTIONS

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BIOASSAY REQUIREMENTS FOR ^{125}I AND ^{131}I

1. SCOPE OF DOCUMENT

The more widespread use of radioactive isotopes of iodine (collectively referred to as radioiodines) as a research tool, coupled with their diagnostic and therapeutic uses in nuclear medicine, has resulted in an increased number of personnel who are exposed to these radioisotopes and who therefore should be monitored for internal radioiodine contamination.

This document describes the minimum acceptable features of a bioassay programme which the Atomic Energy Control Board (AECB) requires to be available in institutions holding a prescribed substance licence[1] authorising the use of significant quantities of ^{125}I or ^{131}I or both (see Table 1). A licensee may submit details of his own proposed bioassay programme to the AECB for approval. If such a programme fails to be approved, the programme described below shall be adhered to. (See Figure 1.) This document does not deal with individuals who are likely to maintain a significant chronic thyroid burden of radioiodine.

It is assumed that the radioiodine taken into the body is in a soluble, inorganic form (I_2, iodide or iodate) or in an organic form (e.g. methyl iodide) which is metabolised in the body with a resultant release of iodide. Radioiodinated organic compounds which are not catabolised to iodide in the body to any significant degree are not the subject of this document, since the metabolism of the radioiodine will be dictated by the metabolism of the compound. This means that individuals whose only exposure to radioiodine is in the form of prepared radioiodinated compounds such as antigens and antibodies (e.g., individuals using radio immuno assay kits in which the antigen or antibody is supplied as radioiodinated material) are not required to participate in this bioassay programme for radioiodine.

Enquiries on bioassay requirements for other radioiodines should be directed to the Radioisotopes and Transportation Division, Atomic Energy Control Board, P.O. Box 1046, Ottawa, Ontario, K1P 5S9, telephone no. (613) 995-1473. It should be noted that advice on comprehensive bioassay requirements for radioiodines is being prepared by a Federal-Provincial group working on bioassay requirements.[2] The reader should also be aware that other regulatory guides may exist or be in preparation that address other specific dosimetry programs, both external and internal, as well as the broad aspects of dosimetry programs in general such as quality assurance, dose records and approval procedures. The AECB should be consulted to see which guides are appropriate for a particular licensed operation.

A glossary of terms is appended (Appendix D).

2. INTRODUCTION

Many of the uses of radioiodine involve the manipulation of open sources with the attendant hazard of volatile radioiodine being released to the work environment. While safe working procedures (see Appendix A) will minimize the likelihood of radioiodine being ingested, inhaled or absorbed, it is necessary to ensure that adequate precautions are being taken. Detection of significant levels of radioiodine in the body or body fluids may serve as a warning that working conditions or procedures are potentially unsafe. Routine bioassays for radioiodine will therefore play an important role in a comprehensive radiation safety programme.

The Atomic Energy Control Regulations[1] limit the maximum permissible dose of ionizing radiation that an Atomic Radiation Worker[1,3] may receive to the thyroid to 30 rem/year (300mSv/year)*, while the thyroid of a member of the general public may receive only 3 rem/year (30mSv/year)* and that of an individual under the age of 16 years is further restricted to 1.5 rem/year (15mSv/year)*. Any organization employing people who may be subjected to significant levels of radioiodine must, therefore, have some method of detecting radioiodine in the body to ensure that maximum permissible doses to the thyroid are not exceeded.** The limitation of the dose to the thyroid is expected to change as part of a general revision of Section 19 of the Atomic Energy Control Regulations, presently being released for public comment, and therefore corresponding changes in bioassay requirements will be necessary.

Although the doses per unit activity per day (see Table 2) are markedly different for ^{125}I and ^{131}I, the committed dose equivalents per unit activity differ by less than 25% due to the difference in physical half-lives for the two radioisotopes. This is reflected in the recommendations spelled out in Publication 30 of the International Commission on Radiological Protection[4] where the annual limits of intake for ^{125}I and ^{131}I are identical. In practical terms, the similarity of committed dose equivalents means that the two radioisotopes can be treated as similar for the purpose of this document. The difference in frequency of bioassay outlined below is due solely to the difference in physical (and therefore effective) half-lives.

Guidelines for medical action in the event of a large intake of radioiodine should be drawn up in consultation with a physician. Prompt action (e.g., administration of potassium iodide) following an intake may minimize the uptake of radioiodine by the thyroid, but such action should only be taken under the direction of a physician.

3. ESTIMATION OF THYROID BURDEN

Iodine is concentrated in the thyroid gland and is eliminated from the body mainly by urinary excretion. The two main methods of bioassay for radioiodine are direct estimation of organ burden by detection of radiation emanating from the thyroid, and measurement of urinary levels of radioiodine. Although urinalysis for radioiodine is an acceptable method of screening for radioiodine intake, it cannot be used satisfactorily to estimate thyroid burdens in most instances.

It should also be noted that patterns of iodine excretion vary markedly from person to person depending on diet, age, drugs being taken, and other factors. Wherever possible, the measured maximum thyroid burden and calculated retention function for the individual shall be used to estimate the committed dose for that individual. The committed dose shall be calculated, and the results recorded (see Appendix B), if an individual has a detected thyroid burden at, or above, the appropriate investigation level.

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*1 mSv (millisievert) = 100 millirem.

**It should be noted that the dose of ionizing radiation received by the thyroid should take into account external radiation as well as an internal component from radioactive material in the thyroid.

3.1 Direct Estimation of Thyroid Burden

The thyroid gland is an H-shaped organ in the neck slightly above the sternal notch (see Figure 2). The depth of the gland beneath the surface of the neck is variable[5], and therefore detector response may vary from subject to subject depending on the degree of attenuation by the tissue overlying the thyroid gland. This is especially important for ^{125}I which, because of its decay by electron capture and subsequent emission of weak X-rays (30keV max.), is susceptible to large estimation errors due to such variation in degree of tissue attenuation. Direct measurement of radioiodine levels in the thyroid can be achieved by use of equipment capable of detecting the gamma radiations of the radioiodine of interest. Equipment used to detect radioiodines in the thyroid should be calibrated for the isotope of interest under conditions mimicking the thyroid in the neck. It should be noted that instrumentation appropriate for the detection of ^{125}I (e.g., thin sodium iodide crystal) is not necessarily appropriate for the efficient detection of ^{131}I - and vice versa. The sensitivity of the detector can be calculated by taking the count rate shown on the detector and dividing by the known amount of the radioiodine in the phantom in becquerels (disintegrations per second). If one uses the same set-up when measuring thyroid burdens in humans, the sensitivity as determined above can be used as a reasonable approximation. To minimize errors, a standard procedure for performing measurements should be followed. (See Reference 6.)

3.2 Calibration

It is projected that reference thyroid phantoms will be available for intercomparison testing under the guidelines of the AECB policy regarding calibration of dose measuring instruments in cooperation with the Radiation Protection Bureau of the Department of National Health and Welfare. It should be noted that phantoms for ^{125}I and ^{131}I are available commercially.

4. BIOASSAY PROGRAMMES FOR ^{125}I AND ^{131}I

4.1 Participation

4.1.1 Bioassay shall be done when open source quantities of radioiodine exceeding those shown in Table 1 are used. These quantities apply to the total amount of radioiodine used over any three-month period.

4.1.2 People who work with amounts of radioiodine in excess of the quantities shown in Table 1, or who are sufficiently close to the process that significant intake is possible, shall participate in the bioassay programme. The decision to include or exclude individuals will call for familiarity with the specific work conditions at an institution and therefore should be made by the individual(s) designated by the licensee as responsible for radiation safety; if desired, the proposed list of individuals may be checked for suitability by the Radioisotopes and Transportation Division of the AECB.

4.2 Frequency of Bioassay*

The minimum frequencies of bioassay are detailed below.

*Bioassay should be performed after 6 hours but within 7 days following work with radioiodine.

4.2.1 Bioassay for ^{125}I

(a) Routine Status:

An individual is in routine status and shall undergo bioassay after each use of ^{125}I or monthly (whichever is the less frequent),

(i) for the first three months he or she is in the bioassay programme,

(ii) following an observed thyroid burden above the appropriate investigation level (see Table 3),

(iii) following any significant change to radioiodine handling procedures, or

(iv) following any significant increase in amount of radioiodine used.

(b) Maintenance Status:

Bioassay for ^{125}I shall be performed at quarterly intervals if each observed thyroid burden during the previous quarter was less than the appropriate investigation level shown in Table 3. (In practice this will mean that when bioassay for ^{125}I is performed quarterly, any observed thyroid burden above the appropriate investigation level will result in the individual returning to routine status.)

4.2.2 Bioassay for ^{131}I

(a) Routine Status:

An individual is in routine status and shall undergo bioassay after each use of ^{131}I or weekly (whichever is the less frequent),

(i) for the first three months he or she is in the bioassay programme,

(ii) following an observed thyroid burden above the appropriate investigation level (see Table 3),

(iii) following any significant change to radioiodine handling procedures, or

(iv) following any significant increase in amount of radioiodine used.

(b) Maintenance Status:

Bioassay for ^{131}I shall be performed at monthly intervals if each observed thyroid burden during the previous month was less than the appropriate investigation level shown in Table 3. (In practice, this will mean that when bioassay for ^{131}I is performed monthly, any observed thyroid burden above the appropriate investigation level will result in the individual returning to routine status.)

4.2.3 Incidents

A bioassay shall be performed as soon as possible following any incident that might result in a thyroid burden in excess of the appropriate investigation

level shown in Table 3. A follow-up bioassay shall be performed within 24 hours of the incident. If the thyroid burden exceeds the appropriate investigation level, further bioassays shall be performed at ten-day intervals for ^{125}I and two-day intervals for ^{131}I until the thyroid burden drops below the appropriate investigation level. These measurements will aid in estimating the maximum thyroid burden and retention function for the individual and hence the radiation dose received by the thyroid.

4.2.4 Pre-operational and Post-operational Bioassay

Wherever possible, an individual should undergo bioassay prior to beginning work with amounts of radioiodine in excess of the quantities shown in Table 1. This could be associated with a pre-operational radiation safety briefing. The purpose of this bioassay is to ensure that any pre-existing thyroid burden of radioiodine is detected before the person starts working with radioiodine.

Again, if possible, any individual who has ceased to work with radioiodine should undergo bioassay within seven days following the last use of the radionuclide.

4.2.5 Pregnant Workers

Since the foetal thyroid is capable of taking up iodine beginning about the tenth week of gestation[7], and since maximum foetal thyroid doses are about a factor of 2 above those to the mother's thyroid[8], it is appropriate that special consideration be given to bioassay and working conditions of pregnant women.

4.2.6 Records

A written record of bioassay results shall be maintained. (See Appendix B.)

4.2.7 Qualitative Thyroid Checks

It is good practice to check for internally deposited contamination as frequently as practical. For example, it may be possible for personnel to use the contamination monitor in their laboratory for a qualitative thyroid check on each day that radioiodine is used. When this is done, the sensitivity of the contamination monitor should be known to ensure that its use is appropriate (see Section 3). This practice should not replace the bioassay programme described above but rather be an adjunct to such a programme.

4.3 Thyroid Burdens

4.3.1 Investigation Level

If the thyroid burden exceeds the investigation level* of Table 3 but is below the reporting level shown in Table 3 the following action should be taken:

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*If an individual has a chronic thyroid burden greater than the appropriate investigation level (see Table 3), it is probable that the maximum annual permissible dose to the thyroid will be exceeded. The AECB should be contacted (613-593-5408) for advice if an individual shows a thyroid burden greater than the investigation level more than 3 times/year. (Measurements should be more than 15 days apart for ^{131}I and 80 days apart for ^{125}I.)

(a) Restrict the worker from further exposure until the reason for the intake has been investigated and appropriate action taken.

(b) Perform bioassay again, within 24 hours after initial measurements, in order to confirm presence of internal radioiodine.

(c) Carry out repeated measurements at approximately ten-day intervals for ^{125}I and two-day intervals for ^{131}I until the thyroid burden is less than the appropriate investigation level.

(d) Perform bioassays on co-workers, as appropriate.

4.3.2 Reporting Level

If the thyroid burden exceeds the reporting level shown in Table 3, the actions listed in 4.3.1 should be taken and, in addition, the occurrence must be reported to the AECB within 24 hours.

4.3.3 Emergency Procedures (see Appendix C)

(a) Processes carried out in open room or fume hood:

If quantities of radioiodine in excess of 500 megabecquerels* are being used, emergency procedures must be posted in the workplace. If more than 5 gigabecquerels** is being used, the emergency procedures should include access to a physician who can initiate appropriate medical therapy. (See 4.2.3)

(b) Processes carried out in gloveboxes:

If quantities in excess of 50 gigabecquerels are being used, emergency procedures must be posted in the workplace. If more than 500 gigabecquerels is being used, the emergency procedures should include access to a physician who can initiate appropriate medical therapy. (See 4.2.3)

*1 megabecquerel = 27 microcuries

**1 gigabecquerel = 27 millicuries

REFERENCES

1. Atomic Energy Control Regulations Chapter 365 Consolidated Regulations of Canada (1978), amendments SOR/78-58 and SOR/79-422.

2. Pomroy, C.T., "Bioassay Guidelines - Publications of the Federal-Provincial Working Group on Bioassay and In Vivo Monitoring Criteria," Proceedings of the 3rd Annual Meeting of the Canadian Radiation Protection Association, Vancouver, May 1982.

3. Atomic Energy Control Board Information Bulletin 80-3, "Atomic Radiation Workers - Some Questions and Answers", 1980.

4. Annals of the International Commission on Radiological Protection, Vol. 2, Number 3/4, Publication 30, Pergamon Press, 1979, p.88.

5. ICRP, Publication 23 "Report of the Task Group on Reference Man," Toronto, Pergamon Press, 1975, p.196.

6. Brucer, M., "Thyroid Radioiodine Uptake Measurement," ORINS-19, United States Atomic Energy Commission, 1959.

7. National Council on Radiation Protection and Measures (NCRP) Report No. 55, Section 2.2.2.3, 1977, p.9.

8. Johnson, J., Health Physics, 1982, Vol. 43, No. 4, pp. 573-581.

9. Johnson, J., "Annual Limits on Intake and Derived Air Concentrations for the Radioiodines with Mass Numbers from 123 to 135," Atomic Energy of Canada Limited, Document AECL-5701, (1977).

TABLE 1

ACTIVITY LEVELS ABOVE WHICH BIOASSAY FOR ^{125}I OR ^{131}I IS NECESSARY

Types of Operation	Activity Handled in Unsealed Form Making Bioassay Necessary
Processes carried out in open room*	5 MBq (135 μCi)
Processes carried out in fume hood	50 MBq (1.35 mCi)
Processes carried out within gloveboxes which are ordinarily closed**	500 MBq (13.5 mCi)

*Processes that involve the generation of significant quantities of volatile radioiodine shall not be carried out in an open room.

**Gloveboxes used for processes that involve the generation of significant quantities of volatile radioiodine must be appropriately vented.

TABLE 2

RADIOIODINE DATA[9]

	^{125}I	^{131}I
Radioactive half-life (days)	60.3	8.06
Effective half-life (days)	40	7.6
Dose rate per unit activity in the thyroid (μSv/Bq.day)*	2.0×10^{-2}	1.4×10^{-1}
Time to maximum thyroid burden after acute exposure (days)	1.8	1.2

*1 μSv/Bq.day = 3.7 rem/μCi.day

TABLE 3

INVESTIGATION LEVELS AND REPORTING LEVELS FOR ^{125}I AND ^{131}I FOLLOWING A SINGLE UPTAKE OF RADIOIODINE

	THYROID BURDEN	
	Investigation Levels*	Reporting Levels**
Atomic Radiation Worker	10 kBq	100 kBq
Any other person	1 kBq	10 kBq

*The Investigation Level is the thyroid burden at which a review of handling procedures should be initiated. The committed dose to the thyroid from this burden, if it results from a single uptake of radioiodine, is approximately $1/20^{th}$ of the annual permissible dose allowed under Schedule II of the AEC Regulations[1]. It should be remembered that the measured thyroid burden is not necessarily the maximum burden, as the level of radioiodine in the thyroid varies with time since intake.

**A thyroid burden greater than the Reporting Level necessitates a report to the Radioisotopes and Transportation Division of the Atomic Energy Control Board (613) 593-5408 within 24 hours. The committed dose to the thyroid from this burden is approximately one half of the annual permissible dose allowed under Schedule II of the AEC Regulations[1]. For Atomic Radiation Workers, the Reporting Level represents the maximum permissible dose per quarter of a year.

FIGURE 1: FLOWCHART OF BIOASSAY PROGRAMME

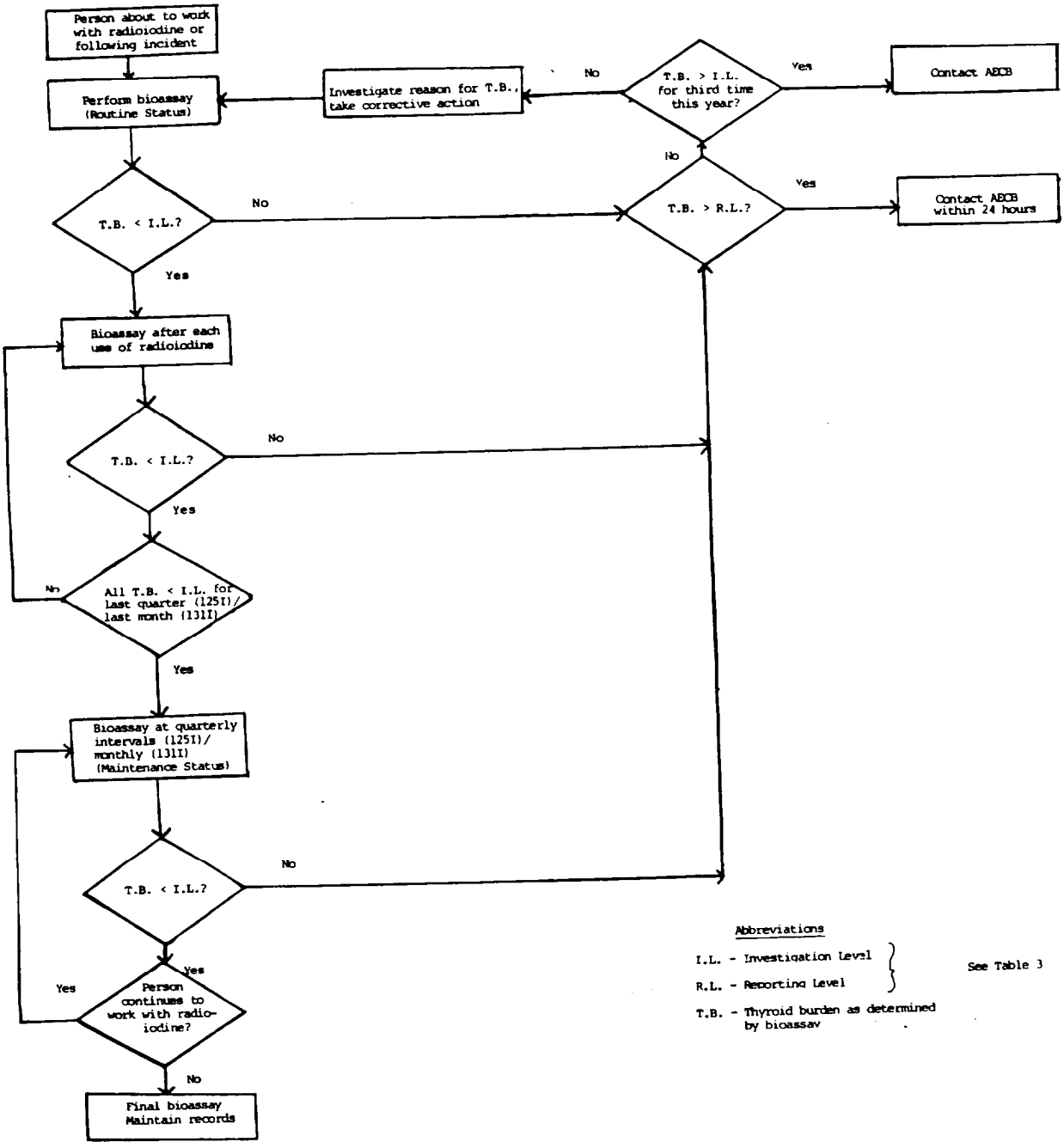
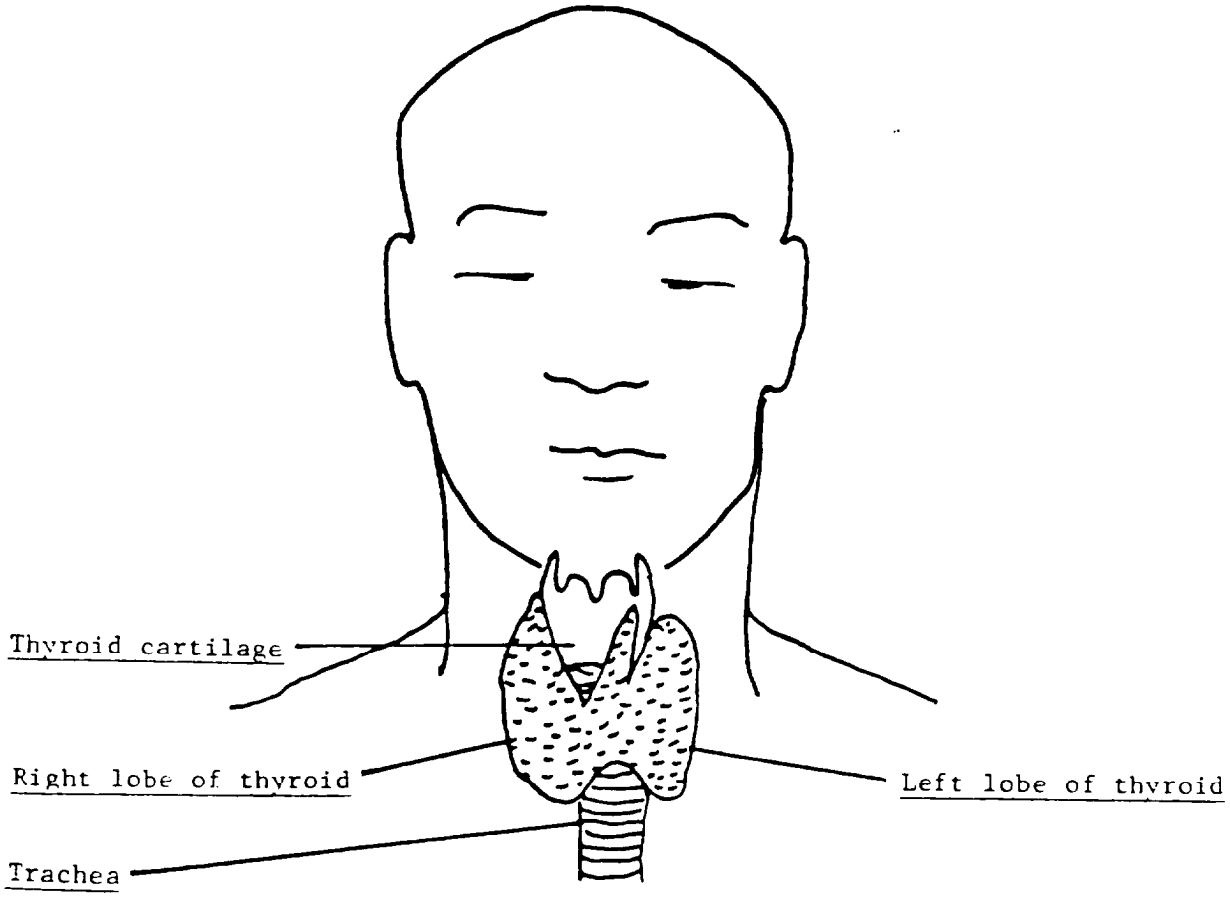


FIGURE 2: LOCATION OF THE THYROID GLAND



APPENDIX A

SUGGESTED PROCEDURES TO BE FOLLOWED WHEN WORKING WITH RADIOIODINES

1. Wear a lab coat, safety glasses and two pairs of disposable gloves. Change if contamination is suspected.

2. On receipt from supplier, check iodine container for significant contamination by wiping outside of primary container and measuring level of radioactivity on the wipe.

3. Wash hands immediately following work with radioiodine.

4. Work in fume hood which has a non-turbulent linear flow rate of between 30 and 60 metres per minute (100-200 linear feet per minute).

5. Vials containing radioiodine should be opened in a fume hood. If a fume hood is unavailable, use a syringe through the rubber stopper of the vial to withdraw the required amount of liquid.

6. Keep containers of radioiodine capped as much as possible.

7. If waste contaminated with radioiodine is to be stored, it should be in a fume hood or other well ventilated area, with appropriate shielding to reduce the dose rate at the working location to less than 2.5 μSv/h.

8. Wherever possible keep the pH of radioiodine solution above pH 8 to minimize production of vapours.

9. Monitor carefully for contamination using appropriate detection equipment.

10. Clean up spills of radioiodine with a solution of 0.1 M sodium iodide, 0.1 M sodium hydroxide and 0.1 M sodium thiosulphate.

11. Avoid direct contact with unshielded containers of radioiodine.

12. Use shielding material and minimise the time spent in close proximity to radioiodine, in order to limit the dose of external radiation.

13. Participate in the bioassay programme as set out in this guide.

DATA TO BE INCLUDED ON BIOASSAY RECORD FORM

Name, date of birth and sex.

Radioiodine checked for and efficiency of detection system for that radioisotope.

Adequate space should be left for comments on factors that may affect the bioassay result, e.g., medication, nuclear medicine procedures and any other pertinent information such as pregnancy.

For each measurement, note the date radioiodine was last handled, the date of measurement, measurement in counts per minute from thyroid, and background counts per minute.*

If the individual has a thyroid burden at, or above, the appropriate investigation level (Table 3), the committed dose shall be calculated and the result recorded.

*Background counts per minute obtained by measuring on arm or thigh to correct for radioiodine in the circulatory system and body tissues other than thyroid.

POINTS TO BE COVERED BY POSTED EMERGENCY PROCEDURES
(SEE 4.2.4, 4.3.3)

1. Phone number of Radiation Safety Officer (R.S.O.)
2. Phone number of physician (if appropriate - see 4.3.3).

Minor Spills

- Inform co-workers.
- Cover liquid with absorbent paper.
- Delineate outer area of spill.
- Decontaminate, taking care not to spread contamination.
- Wipe test for residual loose contamination - acceptable levels should be less than twice background.
- Repeat decontamination until wipe tests show acceptable levels of contamination.
- Survey for fixed contamination - if any is detected, contact R.S.O. for advice.
- Submit written report of incident to laboratory supervisor and R.S.O.
- Consult R.S.O. to determine need for bioassay.

Major Spills (e.g., involving contamination of personnel, release of volatile material)

- Evacuate laboratory, contact R.S.O. immediately.
- Stop any operations that may worsen the situation.
- Leave fume hood running.
- Ensure people leaving the laboratory stay in the immediate vicinity until monitored (N.B. footwear).
- Decontaminate skin with copious quantities of tepid water, followed by soap and water. Do not abrade the skin.
- Post warning signs to prevent entry into contaminated area.
- The R.S.O. will direct clean up operation.
- All occupants of the laboratory should undergo bioassay.
- Submit written report to the R.S.O.
- The R.S.O. should submit a written report to the AECB.

Notes:

(1) The points listed above are suggestions only; emergency procedures should be worked out at the place of use by individuals familiar with work procedures and hazards peculiar to that workplace.

(2) Major and minor spills have not been defined, as circumstances will dictate action. The individual responsible for generating Emergency Procedures should make this decision and provide criteria.

(3) If it is deemed likely that an overexposure has occurred, the AECB shall be contacted within 24 hr. of occurrence as laid out in Section 21 of the Atomic Energy Control Regulations.[1]

APPENDIX D

DEFINITION OF TERMS

Bioassay: The detection of internal contamination by the measurement of radioactivity in biological samples or by direct in vivo measurement.

Biological halflife: The time in which half the atoms of a nuclide are eliminated from the body or organ.

Committed dose equivalent: The total dose equivalent averaged throughout an organ or tissue in the 50 years after intake of a radionuclide into the body.

Effective halflife in the thyroid: A function of the physical halflife and the biological halflife in the thyroid.

Intake: The amount of radioactive material entering the body via nose, mouth or wound or absorbed through the skin.

Investigation level: Value of dose equivalent or uptake above which the results are considered sufficiently important to justify further investigations.

Open source: A source from which radioactive material can readily be removed or escape.

Organ burden: The amount of radioactive material in a specific organ.

Physical halflife: The time in which half the atoms of a radionuclide are transformed through radioactive decay.

Radioiodine: For the purposes of this document, this term is used in a generic sense to include radioactive iodide, iodate or elemental iodine.

Shall, must: Used to designate actions essential to the bioassay programme.

Should: Used to designate actions which are recommended but not essential.

Uptake: The amount of radioactive material absorbed from the extracellular fluid by an organ and deposited within that organ.