FERMILAB-PUB-20-562-DI

Assessing potential induced radioactivity in materials processed with X-ray energy above 5 MeV: Assessment protocols and practical experience

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Abstract

In accordance with ISO11137-1 section 5.1.2, 'the potential for induced radioactivity in product shall be assessed'. This article describes how compliance to this requirement may be achieved using qualified test methods. Materials of consideration are conceptually discussed. Results of testing conducted on products processed with a 7.5 MeV X-ray irradiation process are provided. As X-ray becomes more widely used in healthcare sterilization, having standard assessment protocols for activation coupled with a shared database of material test results will benefit all healthcare product manufacturers seeking to avail of this innovative technology.

This manuscript has been authored by Fermi Research Alliance, LLC under Contract No. DE-AC02-07CH11359 with the U.S. Department of Energy, Office of Science, Office of High Energy Physics.

1. Introduction

Radioactive material of natural origin is ubiquitous in nature, widely varying in type and amount. Energy from these materials, plus radiation of cosmic or cosmogenic origin, is collectively called background. Artificial radioactivity occurs when some human operation results in radioactivity where it was not previously present. Assessment of induced radioactivity in radiation-sterilized healthcare products must determine whether such activity is present at a level higher than background.
In terms of medical device manufacture and sterilization, induced radioactivity must be considered from both a manufacturer employee and a patient end-user perspective

Two broad categories of exposure pathways can be considered for potential risk to individuals[8]:

1. External exposure, i.e., radiation from sources outside the person's body, may be of concern for persons working in the irradiator or distribution warehouse or involved in transporting materials and for health care workers, e.g., physicians and nurses, who handle the product.
2. Internal exposure, i.e., radiation from sources inside the person's body, would occur with patients into whom irradiated products would be placed.

In previous evaluations of induced radioactivity in radiation-sterilized healthcare products[7,8,2] , the estimated or measured concentrations of induced radioactivity is small, generally not distinguishable from background for external exposure. As such, hazards from external radiation would not exist from induced radioactivity in radiation-sterilized healthcare products.

ISO 11137 Standard (Part 1 §5.1.2)[3] requires an evaluation of a potential activation of materials with X- Ray irradiation exceeding 5 MeV.

2. Activation principle

When a photon strikes a nucleus, a particle can be ejected from the nucleus if its binding energy is less than the absorbed photon energy. The remaining nucleus may be radioactive. The main major reaction that can lead to photon-induced activities are:

- The photoneutron reaction: absorption of a photon and expulsion of a neutron
- The photon-proton reaction: absorption of a photon and expulsion of a proton $^{1}H^{+}$
- The photon-deuterium reaction: absorption of a photon and expulsion of a nucleus of deuterium $^{2}H^{+}$
- The photon-tritium reaction: absorption of a photon and expulsion of a nucleus of tritium $^{3}H^{+}$
- The photo-alpha reaction: absorption of a photon and expulsion of an alpha particle, the nucleus of Helium $^{4}H^{++}$

For incident photon energies of 10MeV and below, the photoneutron reactions are most probable, while the emission of other particles become important at higher energy[4]

In a 7.5 MeV X-Ray irradiator, the energy of the high-energetic photons can generate a low neutron radiation during their interaction in the matter (photonuclear effect X,n – see Figure 1).

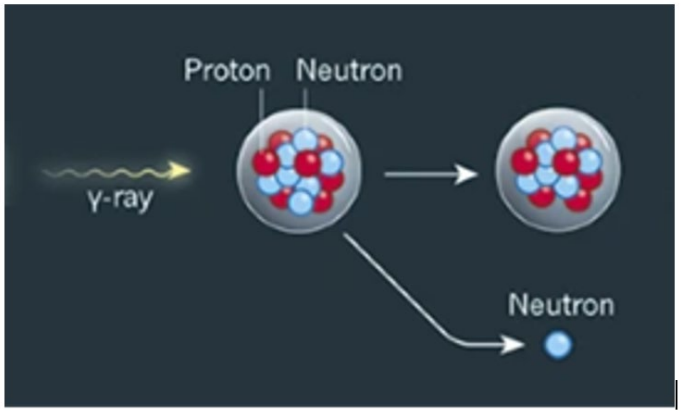


Figure 1: Principle of photonuclear effect (X,n)

For a photon-neutron reaction to occur, the photon must strike a nucleus with more energy than the binding energy of the atom.
This reaction requires at least 2.22 MeV (for hydrogen) and about 10 MeV for the heaviest nuclei.
Figure 2 shows the photonuclear cross section as a function of the energy of the photon. The blue area indicates the X-Rays energy spectrum in a 7.5 MeV irradiator. The proportion of 7.5 x-ray photons from an industrial irradiator that is greater than the threshold energy is limited.

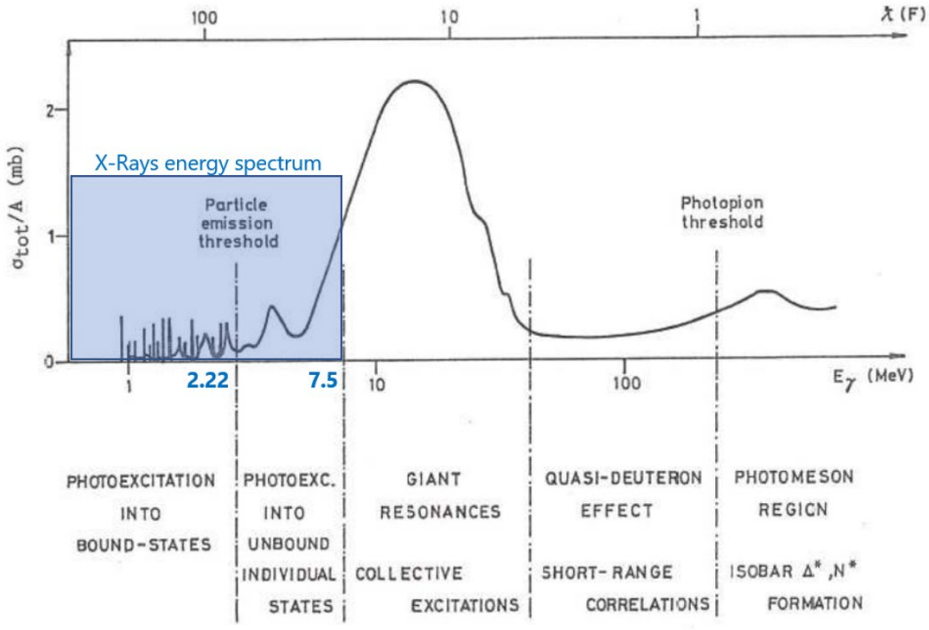


Figure 2: Total photonuclear cross section as a function of the photon energy[6]

Photoneutron activation is the process in which neutron radiation induces radioactivity in some materials, and occurs when atomic nuclei capture free neutrons, becoming heavier and entering excited states.
The excited nucleus, as shown in Figure 3, decays immediately by emitting particles and gamma rays.

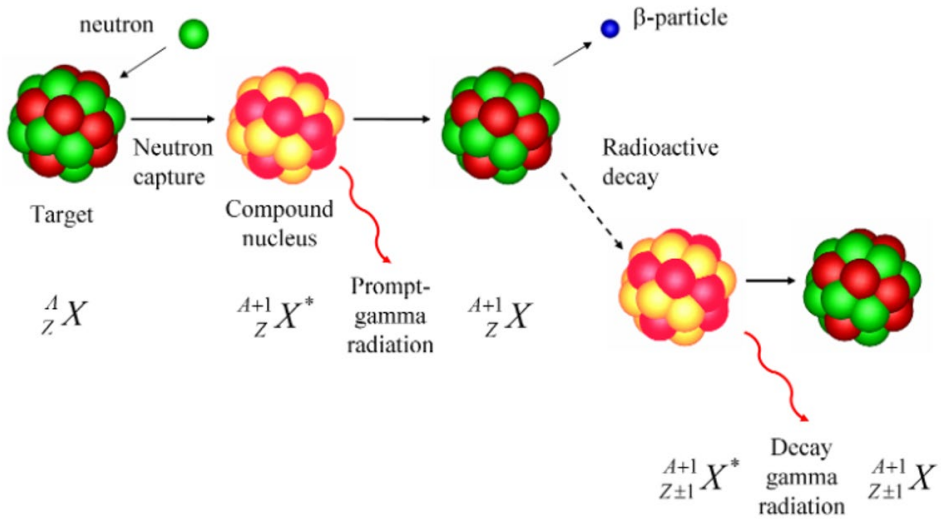


Figure 3: Principle of neutron capture

3. **Assessment of activation based on material composition**

An activation reaction produces a new isotope of either a new element, if a proton was emitted, or of the original element, if a neutron was emitted. Each isotope has a unique threshold energy for such reactions and a particular cross section which determines the probability of the reaction occurring. A list of energy thresholds and an activation risk-based approach according to material composition, X-ray energy, and activation reaction is discussed by Gregoire, et. al.[7]

In order to evaluate the level of concern posed by potential activation by an x-ray beam, a list, Table 1, of elements most likely to be found in medical devices has been assembled. This list was cross referenced with information found in the IAEA's TECDOC-1287,[4] specifically tables 7, 8, and 9. The TECDOC tables list all the naturally occurring isotopes of these elements, the daughter isotope from both (γ,p) and (γ,n) reactions, along with the threshold energies for each.

If a daughter product of a reaction is stable, or the threshold for such a reaction is above 7.5 MeV, then there is no concern for activation of that isotope by the primary X-ray beam and the cell for that element is dark green if all isotopes meet that criterion. If not, the cross section for the (γ,p) or (γ,n) reaction is evaluated to determine if there was reason for concern. In all the remaining cases, the cross section is too small to be of concern or the threshold of the reaction is below but very close to 7.5 MeV. The percentage of X-rays in this energy range is very small and when coupled with the small cross section, is most likely of negligible concern. These were filled in with light green.

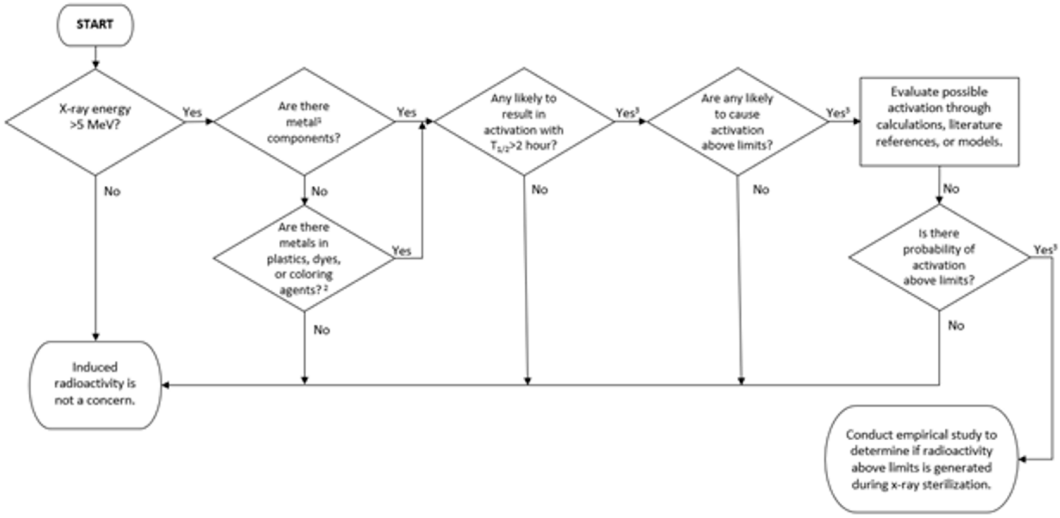
A	Element	Comments
1	H	1
5	B	2
6	C	2
7	N	2
8	O	2
9	F	2
11	Na	2
12	Mg	2
13	Al	2
14	Si	2
15	P	2
16	S	2
17	Cl	2
19	K	2
20	Ca	2
21	Sc	2
22	Ti	2
23	V	2
24	Cr	2
25	Mn	2
26	Fe	2
27	Co	2
28	Ni	2
29	Cu	2
30	Zn	2
34	Se	2
40	Zr	2
41	Nb	2
42	Mo	2
47	Ag	2
49	In	2
53	I	2
73	Ta	2
74	W	3
77	Ir	4
78	Pt	4
79	Au	2

Table 1: Analysis of the naturally occurring isotopes of each element
Comments:
1 - Deuterium is only concern, but is present with only 0.015% natural abundance
2 - All thresholds are greater than 7.5 MeV and/or daughter products are stable
3 - (γ,p) cross section very small, (γ,n) threshold very close to 7.5 MeV
4 - (γ,p) cross section very small, (γ,n) threshold greater than 7.5 MeV
The cross sections were obtained from the TENDL-2019 library which can be accessed through the Evaluated Nuclear Data File (ENDF) from either the IAEA or the National Nuclear Data Center (NNDC). The elements typically used for medical devices were compiled by examining the polymers and metals used for devices, implants, or wiring for implantable devices.

Table 1 does not examine neutron-capture reactions. A small number of neutrons can be generated in the X-ray target, deuterium, C-13, or O-17 (0.015%, 1.11%, 0.04% natural abundance for H-2, C-13, O-17 respectively). The capture of these neutrons, resulting in activation, is a second order effect. As such these reactions result in barely measurable activation that is below action levels as can be seen in table 2 to 4 below.

In evaluating potential radiation risk to individuals, the International Atomic Energy Agency (IAEA) Basic Safety Standard (BSS)[10] applies the term exemption to a practice, and sources within that practice, determined *a priori* to meet criteria that would free it from the requirements of the BSS. [IAEA 2004]. The IAEA has published derived concentration levels for a wide range of radionuclides that, based on distribution and uptake models, would be low enough to be considered exempt. Similarly, the United States Nuclear Regulatory Commission (USNRC) published a table at 10 CFR§30.70, Schedule A, of exempt concentrations for a variety of radionuclides, although more limited in scope than the IAEA exemption. To determine whether induced radioactivity exists in sufficient quantities to be of safety concern, the IAEA exempt concentrations provide a sound basis.
Assessing the potential for induced radioactivity in irradiated products should follow a logical sequence, as depicted in the flow chart of Figure 4. The first assessment is simple: if the X-ray irradiator energy does not exceed 5 MeV, no further evaluation is required. In a higher energy irradiator, the assessment should determine whether there are any metal components or constituents

present. Based on published literature[7,8] and previous measurements, the probability of nonmetals being activated at levels exceeding the exemption limit is negligible.



1. The limited number of nonmetals in healthcare product that may be activated during x-ray sterilization have negligible probability of exceeding exemption levels.
2. Many plastics, dyes, and coloring agents contain metal constituents that may activate with x-ray irradiation. If the presence of such agents is unknown, answer "yes" for the evaluation.
3. For these steps, if the response is "unknown" or "indeterminate," answer "yes."

Figure 4: Process for conducting an assessment of the probability of induced radioactivity occurring at levels higher than the exemption limit

It is important to note that if a product contains no metal component (i.e., a part made of metal), it may still contain metal. Various polymers may contain metal constituents, such as (a) certain dyes that may contain metals, including cadmium, chromium, nickel, cobalt, and/or copper,[1] and (b) metal-containing polymers used as drug delivery vehicles, biosensors, and in bioimaging[13], which need to be included in the assessment. For this step and each of the subsequent steps in the assessment, if it is not possible to answer the questions definitively, the more conservative conclusion should be assumed, e.g., if it is unknown whether metal constituents are present , the next step in the assessment should be taken as though the answer had been "yes."

Induced radioactivity will generally not present undue risk to individuals if the half-life of the radionuclide is short compared to the time interval between irradiation and distribution. For example, a radionuclide with a three-hour half-life would decay to 0.4% of its initial activity over a 24-hour period. During that same period, the activity of a radionuclide with a two-hour half-life would reduce to 0.02% of its initial value. For the assessment described in this paper, if the induced radioactivity half-life is less than two hours, the potential for exceeding the exemption limit was considered negligible.

The final step of the initial evaluation is to determine whether, based on published literature or previous measurements, irradiation of the product may result in induced radioactivity greater than the exemption limit. If a reasonable expectation exists, further evaluation should be made to determine the probability that irradiation of this particular product results in elevated induced radioactivity. This evaluation may be a more detailed search of available data or case histories, calculations specific to the circumstances, or more detailed mathematical modeling. If there remains a significant probability that induced radioactivity could exceed the exemption level, empirical evidence should be gathered by irradiating the product and measuring induced radioactivity.

4. Methodology of activation assessment

To make an empirical evaluation or measurement of the presence of induced radioactivity in irradiated products, two approaches may be taken:

1. perform a screening measurement of the product to determine whether radiation emissions exceed background, which would indicate the presence of radioactivity, if protocols for using the screening instrument ensure the ability to detect radioactivity at the exemption level.
2. perform qualitative and quantitative analysis of the product to determine which radionuclides are present and in what quantity, values for which can be compared against the specific exemption level for the radionuclides detected in the sample

The activation of elements is proportional to the absorbed dose received, this means that if the absorbed dose received (in Gray) doubles, the activity of an activated radioelement (in Becquerel) also doubles

Screening method:

The Ludlum model 54A Small Article Monitor shown in Figure 5 is a self-contained radiation detection instrument designed to detect radioactive contamination on objects small enough to fit into the chamber. The active portion is a cubic chamber lined on six sides with plastic scintillators, providing 4-π counting geometry. Figure 6 shows the monitor with an internal sample holder designed to position a check source in the center of the counting chamber.
The minimum detectable activity for this method was established as the critical level, L_C, which is the signal level above which an observed instrument response may be reliably recognized as "detected above background."[12] This minimum detectable activity must be compared against a target value from the IAEA and USNRC tables of exempt radionuclide concentrations. Taking the lowest value for any exemption level in the tables and assuming a minimum mass for the product being irradiated, the activity target for the screening instrument can be calculated. Figure 7 depicts results of an experiment to establish the critical level as a function of count time. The independent variable is the ratio of the critical level against the derived exemption limit. For this situation, a count time of approximately eight minutes gives a critical level equal to the exemption limit.

Based on validation tests conducted on the instrument, a routine procedure was established to assess the potential for induced radioactivity in products irradiated in x-ray. The important steps are

1. Irradiate the sample to a dose higher than the maximum acceptable dose of the device (worst case approach)
2. The default count time is 10 minutes, corresponding to L_C approximately 14% below the exemption level.
3. Prior to making an irradiated-product measurement, conduct a ten-minute empty-chamber count to monitor consistency and reproducibility of local background, similar to a statistical process control chart.

4. Prior to making an irradiated-product measurement, perform a count of a radioactive source of known low activity, i.e., activity similar to levels that might occur for induced radioactivity.
5. Count the irradiated product. If the count exceeds L_C, conduct another count after an interval equivalent to the expected operational time between irradiation and product shipment, to determine whether the radioactivity is short-lived.
6. Assess the potential risk from any induced radioactivity, accounting for the level of activity present and the length of its half-life.

Figure 5: Ludlum Model S4A SAM installed at STERIS Libertyville X-ray RTC center

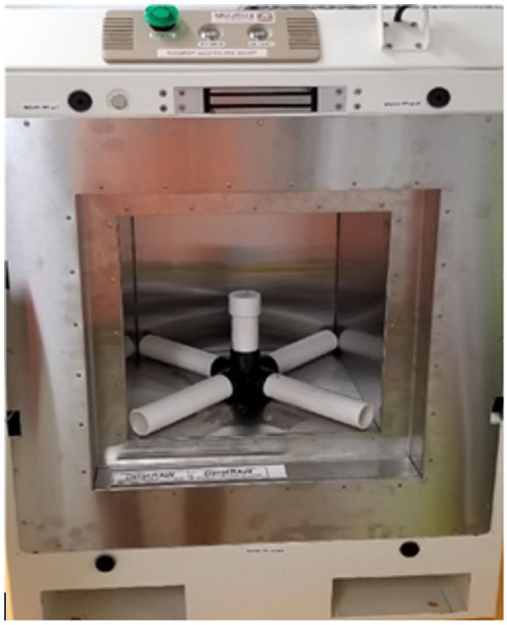


Figure 6: Ludlum Model S4A SAM with source positioning device

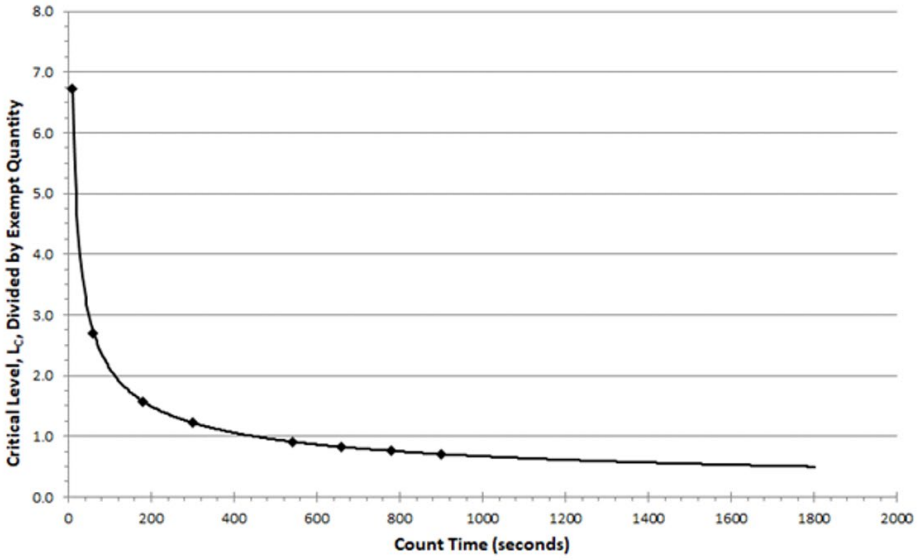


Figure 7: Experiment to establish count time for screening instrument

Qualitative and Quantitative approach

On a regulatory point of view, there is no requirement to know which radionuclide is present in the tested device. It may be interesting to use this method to determine the radionuclide which cause of this activation level when the screening method approach result show an activation level higher than the authorized limit.
Germanium detectors (Figure 8) are used to determined which radionuclide are present and in what quantity.

Due to the complexity of the setup and cost of the spectrometer, the measurement is usually done by an approved laboratory and a certificate is delivered as an output of this measurement.

- Exposed sample to a dose at least higher than the maximal acceptable dose of the device (worst case approach)
- After the process, send the sample to the approved laboratory in the same day.

Note: Start and end exposure time must be recorded as well as minimum and maximum doses received by the sample

- The laboratory performs activation measurement.
- If activation level is detected, the laboratory will define which radionuclide is present and calculate the level of activation at the time of end of the process.

Figure 8: Germanium GeHP spectrometer

5. Case study results

Case study of table 2 are based on qualitative and quantitative method.
The activity (in Bq) has been recalculated at the time of irradiation, following a measurement in laboratory with a Germanium Hyper Pure (GeHP) detector.

Case Study	Product tested	Max Dose received (kGy)	Element	Radionuclid	Max measured activity (Bq)
1	CoCr Heads	49	Chrome	Cr-51	**11.6**
			Cobalt	Co-60	**19.2**
			Molybdenum	Mo-99	**8.0**
2	Laboratory animal feed	90	Sodium	Na-24	**11.4**
3	Surgical Gloves	50	Barium	Ba-135m	**4.8**

Table 2: Case study results

Note: It is unlikely to detect an activated radioelement in polymer products, such as vials, syringes or bottles. Case 3 is therefore an exemption of polymer products for which an activation was detected.

Summary of results found at STERIS Daeniken

Table 3 lists all the radionuclides that were detected in product samples, their associated regulatory limit and half-life:

Element	Radionuclid	Max measured activity (Bq)	Max acceptable activity (Bq) *	Half-life**
Sodium	Na-24	**129**	**1 000**	15 hours
Chrome	Cr-51	**13.3**	**100 000**	27.7 days
Manganese	Mn-56	**0.7**	**10 000**	2.6 hours
Cobalt	Co-60	**19.2**	**10 000**	5.27 years
Copper	Cu-64	**4662**	**100 000**	12.7 hours
Arsenic	As-76	**1.2**	**10 000**	26 hours
Bromine	Br-82	**1.8**	**1 000**	35 hours
Molybdenum	Mo-99	**8.0**	**10 000**	2.7 days
Tellurium	Te-123m	**0.3**	**1000**	119 days
Barium	Ba-135m	**131**	**100 000**	28.7 hours
Tungsten	W-187	**535**	**10 000**	23.7 hours
Platinum	Pt-191	**2.1**	**10 000**	2.9 days
Gold	Au-198	**1.9**	**10 000**	2.7 days

Table 3: Summary of results found at STERIS Däniken

*Max acceptable activity values are based on the International Safety Standards No 115 set by the IAEA.

** Half-Life: the time required for a quantity to reduce to half of its initial value
For example: Copper-64 (Cu-64) has a half-life of 12.7 hours, which means that after 10 times this period (about 5.3 days), its radioactive activity has been divided by more than 1000 (2^{10}).

These measured activity levels are very low, here are some natural activities in comparison:

- A human body has an average natural activity of 8000 Bq
- 1 kg of granite has a natural activity of approximately 4000 Bq
- A 150 g banana has a natural activity of about 21 Bq

These natural activities come from radioelements with extremely long half-lives such as Uranium 238 (4.5 billion years) or Potassium 40 (1.25 billion years).

Results using a screening method:

The screening method is currently being implemented, such that a minimal number of measurements have been collected. Absent data to establish patterns or trends, the instrument performance can be compared against values reported in table 3.

Accounting for photon yield of radionuclides in Table 3, all of which were detected at levels well below the exemption limit, and comparing the calculated activity to the screening instrument L_C , five radionuclides at the activity listed would have resulted in an instrument measurement above L_C = 7.5 Bq . These results would be considered detection of induced radioactivity from ^{24}Na, ^{60}Co, ^{64}Cu, ^{135m}Ba, and ^{187}W. All other listed radionuclides would have insufficient activity to have exceeded L_C using the screening instrument.

In operations, if induced radioactivity is detected, further evaluation would be needed to assess the potential impact, specifically to determine whether activity exceeds the exemption limit. The first step would be to identify constituents of the material in which induced radioactivity was detected. Gregoire, et. al. provided a basis for this evaluation[7] [. For example, ^{24}Na would be expected in glass, particularly borosilicate glass. ^{135m}Ba may also

occur in glass, as well as certain types of coloring agents. For others, ^{64}Cu is expected in brass, while ^{60}Co could be in stainless steel and ^{187}W in coatings for metallic blades. On the basis of the number and type of measurements reported above, it could be assumed that, if induced radioactivity was detected in these materials, the identified radionuclide is most likely the detected activity. As such, comparison of the activity measured by the screening instrument against the exemption limit for the particular radionuclide would be an evaluation of risk from irradiating that product. In some situations, it might be necessary to conduct qualitative measurements, such as gamma spectroscopy, to determine the specific radionuclide.

6. Conclusion

Assessment of induced radioactivity, as required by ISO 11137-1, requires a methodical approach, based on an understanding of the mechanisms whereby induced radioactivity may occur within a product. The assessment must be based on potential risk to persons from the radioactivity in the product, which can be based on comparison against established exemption limits. While much of the assessment can be based on theoretical considerations, eliminating many materials from consideration due to the low probability of induced radioactivity occurring, some means of measuring the presence of radioactivity will be necessary for verification on some products. This measurement may be a screening method to determine if radioactivity exists above background levels, or a method that provides both qualitative and quantitative analysis of the sample product. A history of making such measurements at an operating X-ray irradiator shows that the majority of products exhibit no induced radioactivity, while radioactivity that has been measured in a limited number of products has been well below the exemption limits.

7. Acknowledgements

The authors would like to thank and acknowledge the Kilmer Collaboration Modalities group for the collaborative efforts considering and exploring how additional sterilization modalities may be deployed and adopted by the healthcare products manufacturing industry, for the benefit of patient care.

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