International Journal of Cell Science & Molecular Biology
ISSN: 2572-1100

Juniper Publishers
key to the Researchers

Review Article
Volume 6 Issue 1 - July 2019
DOI: 10.19080/IJCSMB.2019.06.555680

Int J cell Sci & mol biol
Copyright © All rights are reserved by Jorge Morales Pedraza

The Need to Update the International Atomic Energy Agency Code of Practice for the Radiation Sterilisation of Tissue Allografts

Jorge Morales Pedraza*

Consultant on International Affairs and former IAEA Senior Manager, Austria

Submission: July 03, 2019; **Published:** July 18, 2019

***Corresponding author:** Jorge Morales Pedraza, Consultant on International Affairs and former IAEA Senior Manager, Austria

Abstract

The International Atomic Energy Agency (IAEA) adopted in 2007 the current text of the International Atomic Energy Agency Code of Practice for the Radiation Sterilisation of Tissue Allografts (IAEA Code of Practice) after several years of the work of a group of international experts under the supervision of the IAEA Secretariat. The IAEA Code of Practice sets out the main requirements to ensure that the radiation sterilization of tissues produces sterilized tissue allografts suitable for its safe clinical use. The IAEA main contribution to the process of human tissue sterilization is the development of the guideline for the proper use the ionizing radiation technique for tissue sterilization a method used today by many countries from different regions as a result of the use of this technique [Foot note 1].

Keywords: Ionizing radiation; sterilization of tissues; IAEA code of practice; IAEA; Radiation dose

Introduction

The International Atomic Energy Agency (IAEA) program on radiation and tissue banking was one of the most comprehensive programs of the IAEA within its Technical Cooperation Department until its closure in 2005. This program has been previously described in detail in [1,2] and later in [3]. At the beginning of the implementation of this program the IAEA Secretariat promoted, during the period 1960s-1970s, the use of the ionizing radiation technique for the sterilization of health care products and medical devices in several IAEA member states [4]. Later during the 1980s, and as a result of the successful use of the ionizing radiation technique for the sterilization of health care products and medical devices by a group of IAEA member states the IAEA Secretariat started to consider the possibility to use the ionizing radiation technique for the sterilization of human tissues. The IAEA stressed that the use of this technique should be done following strict guidelines for donor selection and graft processing, all conducted within an overall quality system for which strict operational standards were specified [5]. During the 1980s, 1990s, and 2000s, the IAEA Secretariat tested and confirmed exhaustively that the sterilization of human tissues using the ionizing radiation technique, if specific conditions are met and the proper radiation dose is delivered, offers a clear advantage regarding safety compared with other sterilization techniques in use in different countries for the above specific purpose [6]. After several years of preparation within a group of international experts selected by the IAEA Secretariat, the IAEA adopted in 2007 and published in 2008 the final version of a code of practice for the sterilization of human tissues entitled "Radiation Sterilisation of Tissues Allografts: Requirements for Validation and Routine Control" under the technical supervision of the IAEA technical officer Jolyon Hendry.

Main Reasons for the Preparation of the IAEA Code of Practice

The IAEA Code of Practice was prepared with the aim of including specific requirements that need to be observed by all tissue banks that use the ionizing radiation technique for human tissue sterilization. The purpose of this document is to ensure that a radiation sterilization dose selected for sterilizing a specific tissue produce a tissue that can be used safely in specific medical treatment [7]. Before the adoption of the IAEA Code of Practice in 2007 the document ISO 11137 (1995) [8] was used as a reference

1. Jorge Morales Pedraza, Consultant on International Affairs, Senior Consultant in Morales Project Consulting, and former IAEA Senior Manager, Vienna, Austria- First page

to select and validate radiation doses used for human and animal tissue sterilization using the ionizing radiation technique by some IAEA member states. However, it is essential to single out that the document mentioned above was prepared as a guide for the sterilization of health care products and medical devices, which have different technical characteristics than human and animal tissues [7]. Although the principles adopted in the IAEA Code of Practice are similar to those used for the sterilization of health care products and medical device "there are substantial differences in practice arising from the physical and biological characteristics of tissues" [9].

One of the main problems with the use of the document IS`O 11137 (1995) for human tissue sterilization is the application of Methods 1 and 2 included in this document. It is important to recall that these methods were prepared to be applied to the sterilization of health care products and medical devices and not of tissues. Both methods required the use of a high number of samples, and this is very difficult to have in the case of human tissues. It is well known that the availability of processed tissues per production batch is always minimal and usually in various sizes and shapes [7]. For a reason mentioned above and to apply these two methods for human tissue sterilization, substantial modifications were necessary to introduce in those methods to allow the use of a low number of human tissues allograft samples.

Main Issues to be Considered During the Revision of the Current Text of the IAEA Code of Practice

A summary of the issues to be considered and eventually included in a revised text of the IAEA Code of Practice can be found in the following paragraphs.

The appropriate radiation dose for tissues sterilization

Knowledge of the number and resistance to radiation of the microorganism population in the tissue allografts to be sterilized shall be obtained and used for determination of the appropriate sterilization dose to be given to the tissue. For this reason, specific studies should be supported by the IAEA to confirm principles and practices recommended by the IAEA in the current text of the IAEA Code of Practice. The outcome of these studies should be included during the preparation of the revised version of the current IAEA Code of Practice. The aim of this process is "to establish the types of microorganism that are normally found on the tissue types to be sterilized as well as their numbers and resistance to radiation. Such studies should take account of the distribution of the microorganisms within the tissue allograft itself, since this may not be uniform" [9].

Tissue banks operating in countries where the ionizing radiation technique is used for the sterilization of tissues applied different sterilization dose. The IAEA suggested for the sterilization of tissues, to use a sterilization dose of 25 kGy but after a strict tissue processing within the tissue bank. The use as a reference of the documents ISO 11137 (1995) and ISO/TR 13409 (1996) to validate the process of tissue sterilization using the ionizing radiation technique, was a major concern within for the IAEA Secretariat. The reason for this concern is straightforward: the population (type and distribution) of microorganisms and levels of bioburden in tissues are different from the ones that can be found in health care products and medical devices [7]. The levels of microbial contamination in health care products and medical devices are usually much lower than in tissues. Also, the processed tissues are relatively not uniform in size and density [10], which is not the case considering health care products and medical devices.

The current version of the IAEA Code of Practice recommends a standards radiation target dose of 25 kGy for the sterilization of tissues. However, there are several opinions regarding the level of the radiation dose to be given to specific human and animal tissues for sterilization purpose that need to be seriously studied by the IAEA. Some countries believe that for tissue sterilization a radiation dose higher than 25 kGy should be selected, while other countries think that a radiation dose lower than 25 kGy for specific tissues and conditions should be more than enough. Two methods are available in the current text of the IAEA Code of Practice for the determination of a radiation dose for tissue sterilization purposes. The main limitation of these two methods is that the selection of the radiation dose is based on statistical approaches that have been established for the sterilization of health care products and medical devices as previously described in the following documents [7]: ISO 11137 (1995) [8], ISO/TR 13409 (1996) [11], ISO/TR 15844 (1998) [12] and AAMI TIR-27 (2001) [13] but not specifically for tissue sterilization [Foot note 2-Foot note 5] .

2. Other methods of human tissue sterilization using heat and chemicals have also been practiced in some countries for a long time. It has been demonstrated that the sterilization of human tissues using heat and steam techniques could damage the tissue's biological and physical properties or composition, whilst sterilizing it with ethylene oxide gas leaves toxic residues that warrant quarantine period before the sterile products can be used [10]. - Third page

3. The final text of the IAEA Code of Practice "was discussed extensively at an international meeting in Wexham in the United Kingdom and was approved by the Technical Advisory Committee of the IAEA program on radiation and tissue banking, which included the Chairpersons of the American Association of Tissue Banks, the Asia–Pacific Surgical Tissue Banking Association, the European Association of Tissue Banks and the Latin American Association of Tissue Banking" [9]. - Third page

4. Experts were nominated by the IAEA Secretariat, and the acitivites carried out by this group were under the leadership of Professor Glyn O. Phillips, acting as IAEA external consultant, and Jorge Morales Pedraza, acting as IAEA Interregional Senior Manager. The main purpose of the IAEA Code of Practice is to serve as a guide "to tissue banking staff, surgeons using tissues for transplantation, regulators who oversee the safety of transplantation and radiation sterilization procedures, members of tissue banking associations, health service personnel in hospitals in which tissue transplantations are performed, and inter-governmental organizations involved in transplantation issues, for example the World Health Organization" [9]. - Third page

How to cite this article: Jorge Morales Pedraza. The Need to Update the International Atomic Energy Agency Code of Practice for the Radiation Sterilisation of Tissue Allografts. Int J cell Sci & mol biol. 2019; 6(1): 555680.DOI: 10.19080/IJCSMB.2019.06.555680

It is well known that all of the documents mentioned above have been replaced by ISO 11137 (2006), a paper that was not possible to use as a reference for the preparation of the current text of the IAEA Code of Practice. For this reason, none of the main principles and recommendations included in the document mentioned above are included in the current text of the IAEA Code of Practice. To solve this problem additional studies should be carried out by the IAEA to consider giving more examples on how the number of samples required for validation purposes can be met and how this limited number of samples can substantiate the radiation dose selected [7]. Besides it is crucial that the IAEA identify which is the appropriate level of the radiation dose that should be given to specific human and animal tissues for sterilization purpose bearing in mind the experience in the application of different levels of sterilization dose delivered to the same type of tissues by several IAEA countries with excellent results.

New processes and advanced technologies

The current text of the IAEA Code of Practice does not include any new processes and advanced technologies registered in the field of tissue banking in the latest 11 years. These new processes and advanced technologies already registered could provide an improvement in tissue quality, washing procedures, and cell and tissue engineering, among others. For this reason, it is vital that the new text of the IAEA Code of Practice should include any new processes and advanced technologies in the field of tissue banking already used by some IAEA member states with excellent results as well as in the use of the ionizing radiation technique for sterilization purposes.

Training of the staff in the irradiation facility

One of the most critical issue to ensure the production of a processed tissue free of contamination disease for its safe use in specific medical treatment is the training of the tissue bank staff and the team of the radiation facility in the use of the ionizing radiation technique and in the application of the IAEA Code of Practice. The current text of the IAEA Code of Practice stresses the importance that the staff of the tissue bank using the ionizing radiation technique is adequately trained not only in the application of this technique but also in the use of the IAEA Code of Practice [7]. However, nothing is said about the importance of training the staff of the radiation facility where the tissue is going to be sterilized in the use of the ionizing radiation technique and the IAEA Code of Practice. The importance of training the radiation facility staff in the use of the ionizing radiation technique and the IAEA Code of Practice is to ensure that it has the necessary skill and qualification to deliver accurate radiation dose during routine sterilization activities [7]. However, the importance of the training of the radiation facility staff is not mentioned in the document cited above. For this reason the IAEA Secretariat should ensure that the revised text of the IAEA Code of Practice includes an explicit reference to the importance of training the radiation facility staff in charge of the use of the ionizing radiation technique for tissue sterilization and in the application of the IAEA Code of Practice.

Validation of pre-sterilisation processes

It is well known that an essential step in the overall radiation sterilization of human tissues is the rigorous donor selection to eliminate specific contaminants. One of the elements in this process is the application of serological tests to the donor to detect possible contaminants that can impede the production of high-quality human tissue. The current text of the IAEA Code of Practice mentioned a group of specific serological tests that need to be applied to the donor to ensure the production of high-quality human tissue. However, it is well known that statutory regulations in some countries may require other serological tests and the detection limits associated with these tests or when particular infections are identified. This specific situation should be studied in detail by the IAEA to decide which new serological tests already applied by some IAEA member states should be included in the revised text of the IAEA Code of Practice to be prepared in the future. In considering such new serological tests due consideration should be given to the detection limits of such tests. It should also be verified that the combination of processing, preservation and irradiation is capable of eliminating or reducing contamination to an acceptable level in the procured tissue [7].

Validation of the sterilization process

The validation of the method used for the sterilization of tissues should be performed by adequate measurements of the absorbed radiation dose set a priori and required to achieve the specified SAL (Sterility Assurance Level). In addition to proper dosimetry systems it is advisable to use radiation-sensitive indicators as stated in ISO 11137 (2006) Part 3 [7]. Several factors not only affect the effectiveness in the use of the ionizing radiation technique for the sterilization of human tissues but can also modify microbial sensitivity to ionizing sterilization. One of these factors is bioburden. The lower the bioburden is the more effective the process will be [7]. The revised text of the IAEA Code of Practice should consider all factors including bioburden, that can modify microbial sensitivity to ionizing sterilization in detail.

Revision of annexes of the current version of the IAEA code of practice

Without a doubt, Annexes 1, 2 and 3 of the current text of the IAEA Code of Practice should also be reviewed in detail by the

5. The variability in types and levels of bioburden in tissues is much greater than that found for health care products and medical devices, "where the levels of microbial contamination are usually low and relatively uniform in type and level". In addition, to what has been said above, "tissue allografts are not products of commercial production processes involving large numbers of samples" [9]. - Third page

How to cite this article: Jorge Morales Pedraza. The Need to Update the International Atomic Energy Agency Code of Practice for the Radiation Sterilisation of Tissue Allografts. Int J cell Sci & mol biol. 2019; 6(1): 555680.DOI: 10.19080/IJCSMB.2019.06.555680

IAEA during the preparation of a revised version of this code. The purpose of this revision is to ensure that all assumptions, formulas, tables included in the current texts of the IAEA Code of Practice are the correct ones according to the experience achieved by a group of countries in the application of this code since its publication in 2008. According to Annex 1 tissue allografts can be prepared from a wide range of tissues. The IAEA, during the revision of the current text of the IAEA Code of Practice should consider in detail the number of samples to be used in the case of tissue sterilization apply bioburden analysis prior to tissue sterilization for the purpose of establishing the appropriate sterilization dose and the distribution of microorganisms throughout the sample. In document ISO 11137 (1995) "the concept of establishing a verification dose for a SAL value that is much higher than 10–6, for example for a SAL value of 10–2, was proposed as an experimental method of establishing the sterilization dose corresponding to a SAL of 10–6. For such verification dose experiments samples of tissue allografts should be taken from production batches and irradiated at the calculated verification dose. In these experiments it is assumed (and this assumption should be demonstrated statistically) that the tissue allograft products are reasonably uniform in shape, size, composition and bioburden distribution" [9] [Foot note 6].

For this reason, it is now time to prove that the assumption made on the experiments mentioned above is statistically correct or identify which are the necessary changes that need to be introduced in the current text of Annex 1 of the IAEA Code of Practice. Annex 1 also includes the procedures for the establishment of the verification dose and identifies three methods to do so. The use of several mathematical formulas should be carefully studied by the IAEA and the group of experts selected for the revision of the current text of the IAEA Code of Practice. These studies aim to confirm the validity of these mathematical formulas applied for establishing specific sterilization doses and other microbial distributions for samples sizes between 10 and 100 units [14-16].

Proposed actions to be taken

The following are the recommended actions that need to be taken by the IAEA Secretariat and interested IAEA member states to carry out the proposed revision process of the IAEA Code of Practice:

1. To discuss this issue by the IAEA Secretariat with interested IAEA member states to include the revision of the IAEA Code of Practice in its program of work for the coming years.

2. To approve a research contract to collect all available data and experience in the application of the IAEA Code of Practice in a group of IAEA member states from all regions.

3. To select a group of international experts to revise the current text of the IAEA Code of Practice and the preparation of a revised manuscript of the code.

4. To submit the revised version of the IAEA Code of Practice to the consideration of interested IAEA member states.

5. To adopt the revised text of the IAEA Code of Practice as an IAEA official document.

Conclusion

Taking into account the importance of the use of the IAEA Code of Practice as a reference by tissue banks and radiation facilities that are using the ionizing radiation technique for sterilization of tissues, it would be imperative that this code is updated as soon as possible. It is crucial not only to revise the code mentioned above by a group of competent experts but to agree that this code should be updated every five years.

Acknowledgment

I want to express my gratitude and thanks to Prof Barry Parson and former IAEA Technical Officer Jolyon Hendry for their opinions on the content of this article.

References

1. Phillips GO, Morales J (2003) The International Atomic Energy Agency (IAEA) program in radiation and tissue banking: Past, present, and future. Cell and Tissue Banking 4(2-4): 69-76.
2. Morales Pedraza J (2006) The IAEA program on tissue banking. A successful program for developing countries; Journal Cell and Tissue Banking 7(4): 237-258.
3. Morales Pedraza, Jorge (2012) The Use of the Ionizing Radiation Technique for Tissue Sterilization: The International Atomic Energy Agency Experience. Nova Science.
4. IAEA Thematic planning reports on tissue banking (1998 and 2007), IAEA, Vienna, Austria.
5. Loty B (2005) IAEA International Standards for Tissue Banks: In Sterilisation of Tissues using Ionising Radiations. Woodhead Publishing and CRC Press, England. pp. 3-38.
6. Yusof N (2001) Effects of Radiation on Microorganisms-Mechanism of Radiation Sterilisation. The Scientific Basis of Tissue Transplantation, World Scientific, Singapore. pp 345.
7. Morales Pedraza J, Norimah, Yusof, Nazly, Hilmy (2011) A review of the International Atomic Energy Agency (IAEA) Code of Practice for the Radiation Sterilisation of Tissue Allografts. Cell Science and Therapy.

6. The objective of the bioburden determination is to:

a. Determine the total number of viable microorganisms within or on a tissue allograft and the packaging after completion of all processing steps before sterilization;

b. Act as an early warning system for possible production problems;

c. Calculate the dose necessary for effective radiation sterilization.

The validation of the bioburden estimation requires determination of the effectiveness and reproducibility of the test method" [9]. – Fourth page

How to cite this article: Jorge Morales Pedraza. The Need to Update the International Atomic Energy Agency Code of Practice for the Radiation Sterilisation of Tissue Allografts. Int J cell Sci & mol biol. 2019; 6(1): 555680.DOI: 10.19080/IJCSMB.2019.06.555680

8. ISO 11137 (1995) Sterilisation of health care products - Requirements for validation and routine control-Radiation sterilisation; International Organisation for Standardisation, Geneva, Switzerland.

9. IAEA (2007) Radiation Sterilisation of Tissue Allografts: Requirements for Validation and Routine Control-A Code of Practice, Vienna, Austria.

10. Yusof N, Hilmy N (2007) Need for Radiation Sterilisation of Tissue Grafts. In Radiation in Tissue Banking, World Scientific, Singapore. pp. 11.

11. ISO/TR 13409 (1996) Sterilisation of health care products - Radiation sterilisation - Substations of 25 kGy as sterilisation dose for small or infrequent production batches. International Organisation for Standardisation, Geneva, Switzerland.

12. ISO/TR 15844 (1998) Sterilisation of Health Care Products-Radiation Sterilisation-Selection of Sterilisation Dose for a Single Production Batch. International Organization for Standardisation, Geneva, Switzerland.

13. AAMI Technical Information Report (TIR)-27 (2001) Sterilization of Health Care Products- Radiation Sterilisation–Substantiation of 25 kGy as a Sterilisation Dose, McLean, Virginia, USA.

14. Silberman F, Kairiyama E (2000) Radiation sterilisation and the surgical use of bone allografts in Argentina. Advances in Tissue Bankingl 4: 27-38.

15. Vangsness C, Triffon M, Joyce M, Moore T (1996) Soft tissue for allograft reconstruction of the human knee: a survey of the American Association of Tissue Banks. Am J Sports Med 24(2): 230-234.

16. Nguyen H, Morgan DA, Forwood MR (2007) Sterilisation of allograft bone: is 25 kGy the gold standard for gamma irradiation?. Cell Tissue Banking 8(2): 81-91.

This work is licensed under Creative Commons Attribution 4.0 License
DOI: 10.19080/IJCSMB.2019.06.555680

Your next submission with Juniper Publishers will reach you the below assets

- Quality Editorial service
- Swift Peer Review
- Reprints availability
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats

(Pdf, E-pub, Full Text, Audio)

- Unceasing customer service

Track the below URL for one-step submission

https://juniperpublishers.com/online-submission.php

How to cite this article: Jorge Morales Pedraza. The Need to Update the International Atomic Energy Agency Code of Practice for the Radiation Sterilisation of Tissue Allografts. Int J cell Sci & mol biol. 2019; 6(1): 555680.DOI: 10.19080/IJCSMB.2019.06.555680