THE IMPACT OF EUROPEAN STANDARDS CONCERNING RADIATION STERILIZATION ON THE QUALITY ASSURANCE OF MEDICAL PRODUCTS IN POLAND

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Abstract

The ISO 11137 and EN 552 standards were issued in the mid-90's. These documents have been devoted to the requirements regarding the sterile medical devices offered on the market. The implementation of those standards by Polish manufacturers of medical devices is discussed in this paper. The currently introduced national regulations effectively stimulated this process. The activities of the Institute of Nuclear Chemistry and Technology (INCT) in the field of radiation sterilization standardization and its radiation sterilization commercial service are described.

1. INTRODUCTION

Radiation sterilization has been applied at the Institute of Nuclear Chemistry and Technology (INCT) since 1973. Till today the only facilities in Poland, where the radiation sterilization is performed in a large scale commercial process, have been built in INCT. The radiation sterilization service was preceded by our investigation of the irradiation conditions (characteristics of the electron beam i.e. beam energy, average beam current, scan width and scan uniformity, conveyor speed) [1] and evaluation of the ionizing radiation dose to obtain sterile medical devices [2]. Our activities in the 80's were supported by the IAEA (through the regional training courses) and based on the AAMI guidelines. After some years of experience, the procedures were written and they became the basis upon which the radiation sterilization process has been carried out. Standardization of the radiation sterilization process in Poland has been initiated recently. This effort is also led by the members of the INCT staff.

2. REGULATORY DOCUMENTS

Our internal procedures were for a long time adequate for us as the contractor and for our customers, but in the mid-90's the international standards concerning radiation sterilization were published (ISO 11137 [3] and EN 552 [4]). It significantly influenced our activity. Also our customers have started to demand service in accordance with these international regulations. All medical devices which are being marketed in Europe must comply with the Medical Device Directive (MDD) [5] and display the CE mark since June 14th 1998. The CE mark provides the assurance to the patients and the users that the products perform as intended by the manufacturer and they are safe when used as intended. The CE mark must be placed visibly, legibly and indelibly not only on all devices or their packaging, but also on the instructions for use and sale packaging. Since the CE mark is mandatory in the countries belonging to Common Market, the Polish products must have the CE mark when they are sold in Western Europe. There are also known examples that some importers from non European Community countries require this mark on Polish products, even if this is not needed by law in both countries. The new regulations have stimulated the effort towards process certification and changed the attitude of the staff at all levels to the quality of the service.

The basic requirement for all sterile products is that they are safe for use according to MDD. It is not related to a specific definition of sterility. It may be SAL of 10^{-6}, 10^{-3} or any other level. The label 'sterile' means that there is no risk of infection from the prospective of the users (physicians or patients). In addition, the process of achieving SAL of 10^{-6} is not defined as the method for obtaining a

safe product. The dose required to achieve SAL of 10^{-6} can cause in some cases the material to become brittle, and therefore unsafe for use.

Most medical device manufacturers have adopted a quality system based on EN 46001 or EN 46002, but in addition they must incorporate the requirements of MDD into their procedures. The link between EN 46000 and the MDD is clarified in the note within the clause 4.2.1 of EN 46001, which states that "if this European standard is used for compliance with regulatory requirements, the relevant requirements of the regulations should be included in the specified requirements". Therefore, a Notified Body will require a manufacturer to meet the requirements of the MDD as well as those of EN 46000 before the CE mark is used.

Sterilization is viewed by EN 46000 and the MDD as a high-risk special process which requires validation. The wide use of the harmonized standards, EN 550, EN 552 and EN 554, to show the conformance to the essential requirements also implies that the control and validation techniques must yield the same level of assurance as the harmonized standards, although the standards are not mandatory. Therefore, it became obvious to the INCT staff and our customers that sterilization which has not been validated or when updated procedures or processes have not been used, this may lead to major non-compliance and delay in CE-marking; that was also observed in UK [6]. When a subcontractor is used for a critical process, it is essential that the controls are the same as those for the processes carried out at the manufacturer's site.

Many medical devices manufactures already follow Good Manufacturing Practice (GMP). Also, several ISO 9000 procedures have been applied, in particular, document control, inspection and testing, calibration and most process controls. The manufacturers should follow the procedure of assessing compliance of the products to different standards. These include the standards dealing with validation of the sterilization processes. In the case of radiation sterilization there are two basic documents ISO 11137 [3] and EN 552 [4].

There is only one major difference between these two standards - the definition of sterility. CEN allows only the level of 10^{-6} for the probability of finding a viable microorganism on a sterilized product. Thus, according to EN 556 [7], which describes the requirements for medical devices to be labeled sterile, the product is sterile only when the sterility assurance level (SAL) of 10^{-6} is achieved. On the other hand, ISO supports the notion of dual SALs for sterile health care product depending on the product use: SAL of 10^{-3} for topically applied medical devices and SAL of 10^{-6} for implantable devices. It should mean from a product point of view that there is no risk of infection when the patient uses the product. Based on this definition, ISO 11137 declares a product sterile with SAL of 10^{-6} or 10^{-3}, depending on its use.

The standards concerning radiation sterilization appeared in the mid 90's. These standards give the guidelines on how the validation and the routine control of sterilization using ionizing radiation should be performed. Taking into account already mentioned requirements and different regulations about sterility, it was necessary to establish our national regulations concerning radiation sterilization. Polish Committee of Standardization (PCS) has decided that a Polish representative would participate in ISO/TC 198 Working Group 2 concerning Radiation Sterilization as an observer to have a world wide perspective of the field. The Standardization Working Group for Sterilization, Disinfection and Antiseptics, with the above-mentioned observer as one of the members, has been appointed. Although ISO 11137 covers wider range of products which can be sterilized by radiation and that its implementation would be less expensive than EN 552, it was decided that the Polish translation of EN 552 would become our national standard. The main reason for selecting EN 552 as a Polish standard was our membership in the European Union. This standard has already been translated into Polish and is under the standardization process in PCS. EN 552 provides two approaches for establishing the sterilization dose to achieve compliance with EN 556 and hence provide a SAL of 10^{-6}:

- selection of the sterilization dose capable of achieving compliance with EN 556 by identifying the number of the innate microbial population present on or in the medical devices and its resistance to radiation, or
- the product is treated with a minimum dose of 25 kGy [8].

In the second case, the manufacturer must substantiate the effectiveness of 25 kGy as a sterilization dose. This is a new requirement; in the past, 25 kGy was generally accepted as adequate for the purpose of sterilization and no further investigations were needed. For both approaches, the manufacturer must have an access to a microbiology laboratory.

3. VALIDATION OF RADIATION PROCESS AT INCT

Till now the Polish Authority responsible for the medical devices distribution allows only the traditional approach; the product has to be treated with the minimum dose of 25 kGy. It is obvious that such an approach increases the costs for the manufacturer and decreases the INCT sterilization capacity.

The main issues that need to be resolved are the validation procedure and the traceability of the product. If the manufacturer follows the standardized methods for sterilization validation, the required calculation and the appropriate statistics are automatically considered. If the validation is followed in this way, the sterilization process will result in a sterile product [9]. The traceability of the irradiated product being sterilized is achieved at INCT by through computer that records the data of the irradiation parameters. Special software was designed by the INCT staff to automatically collect the values of the parameters, such as the beam current, energy and conveyor speed, and the data about the customer and product are also entered. The data are printed on the label which is put on each sterilized package. Also, routine dosimeters used during processing are kept for the period of the shell-life of the product.

The release of the radiation-sterilized products relies on dosimetry. Therefore, it is important for our customers that we have dosimetry procedures well documented. Different types of dosimeters are available. Their responses are traceable to national or international standards [10]. The polystyrene calorimeters and the aluminum-wedge energy measurement device were purchased from the High Dose Reference Laboratory (Riso National Laboratory, Denmark) as reference instruments.

The validation of sterilization process also involved much paper work. In the past, many procedures were done without documentation or were not documented properly. At INCT, much effort was placed for changing the attitude of the staff towards establishing the validation process. They had to understand the importance of following the procedures strictly and for documentation. We have organized internal training for all levels of employees to achieve this. Those efforts are still on going. We have established internal audits to ensure that we meet requirements for validation. They also help us to improve our sterilization process procedures. Finally, we validated our sterilization process in the middle of this year. We are aware that it is a 'never ending story'. The manufacturers of the medical devices increase their investment in validation each year; this means that INCT must revise and upgrade the existing instructions and procedures. It will allow us to be in accord with the requirements of EN 552 and have our process of radiation sterilization really validated and in control.

4. CONCLUSIONS

Today we can say that 25 years of INCT activity in radiation sterilization has been very fruitful. Polish manufacturers of medical devices can compete with the products from all over the world. Still much effort must be put to achieve a full compliance with EN 552.

REFERENCES

[1] BULHAK Z., KOLYGA S., PANTA P., STACHOWICZ W., Fifteen years of experience in the sterilization of medical products with the linear electron accelerator LAE-13/9, Radiat. Phys. Chem., Vol.**34**, No.3 (1989) 395-397.

[2] CZERNIAWSKI E., STOLARCZYK L., Attempt to establish the ionizing radiation dose to be used in the sterilization of one-use medical equipment units, Acta microbiologica polonica, Series **B6** (1974) 177-83.

[3] ISO 11137, Sterilization of health care products – Requirements for validation and routine control – Radiation sterilization, (International Organization for Standardization, Geneva, Switzerland), 1995.

[4] EN 552, Sterilization of medical devices - Validation and routine control of sterilization by irradiation (CEN, European Committee for Standardization, Brussels, Belgium), 1994.

[5] Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, Official Journal of the European Communities, No.L 169, 12 July 1993.

[6] JEPSON CH., Achieving the CE mark: Getting it right first time, Medical Device Technology, Vol.**8**, No.7 (1997) 16-19

[7] EN 556, Sterilization of medical devices - Requirement for terminally sterilized devices to be labeled sterile (CEN, European Committee for Standardization, Brussels, Belgium), 1995.

[8] RICHARDS S., EN 552: Validating 25 kGy as a sterilization dose, Medical Device Technology, Vol.7, No.6 (1996) 22-25.

[9] WINCKELS H.W., DORPEMA J.W., Risk assessment a basic for the definition of sterility, Medical Device Technology, Vol.5, No.9 (1994) 38-43.

[10] MEHTA K., KOVACS A., MILLER A., Dosimetry for quality assurance in electron-beam sterilization of medical devices, Medical Device Technology Vol.4, No.4 (1993) 24-29.