^{60}Co gamma radiation for sterilization of alumina column in ^{99}Mo/^{99m}Tc generators: an alternative to moist heat sterilization process

Fukumori, N. T. O.; Martins, P. A.; Osso Jr, J. A.; Matsuda, M. M. N.

Centro de Radiofarmácia, IPEN-CNEN/SP – Brasil

Instituto de Pesquisas Energéticas e Nucleares - IPEN-CNEN/São Paulo/SP – Brasil

ntfukumo@ipen.br, patyosborne@yahoo.com

OBJECTIVES

Products subject to sanitary surveillance, respecting their particularities, must be produced, dispensed, stored and transported so as to have the necessary security for their use and consumption. For injectable radiopharmaceuticals, as the $^{99m}TcO_4^-$ eluate obtained in the ^{99}Mo/^{99m}Tc generator system it is part of the Good Manufacturing Practices (RDC 63, 2009, ANVISA) that in order to be sterile they must be prepared under conditions which exclude microbial contamination. Thus, the sterilization process of the generator components and ^{99}Mo play an important role in ensuring sterility, to promote the complete removal or destruction of several microorganisms, providing a with desirable level of safety, both for the patient and the operator. The use of $^{99m}TcO_4^-$ represents over 80% of diagnostic procedures in nuclear medicine. Currently the sterilization of the alumina column before dispensing ^{99}Mo is performed by moist heat process. The objective of this work was to study the feasibility of sterilization of alumina column by ^{60}Co gamma radiation, as a safe, effective and economically interesting alternative .

METHODS

The bioburden of the generator accessories (generator lids with filter, bungholes, washing system) and alumina columns was determined before sterilization by gamma radiation (^{60}Co).

Three lots of each type of accessory were irradiated with gamma rays at 15, 25 and 50 kGy absorbed doses for stability studies during 6 months. In this period, they were examined monthly parameters as color, elasticity/flexibility, connection and fitting. Non-irradiated materials were also evaluated and referred to as "control".

Thirty columns were irradiated at 10, 15, 25 and 50 kGy absorbed doses and examined for: changes due to the action of gamma radiation on the glass column; the crystal structure of alumina by scanning electron microscopy (SEM), elemental analysis by EDS and X-ray diffraction; weight change in tetrafluoroethylene (Teflon®) by TGA and DSC; visual changes and mechanical resistance of accessories for ^{99}Mo/^{99m}Tc generator; measuring time and elution volume in "cold" systems for elution, as well as sterility, bacterial endotoxins, pH, Al and Mo concentration in the eluates. For confirmation of the ^{60}Co dose applied to the column generator polymethylmethacrylate (PMMA) dosimeters were placed in empty glass columns exposed to 10 and 25 kGy doses. Figure 1 summarizes the tests.

The bioburden for each material was determinated by method 1 of ISO 11137-2:2006 and the verification and sterilization doses were set.

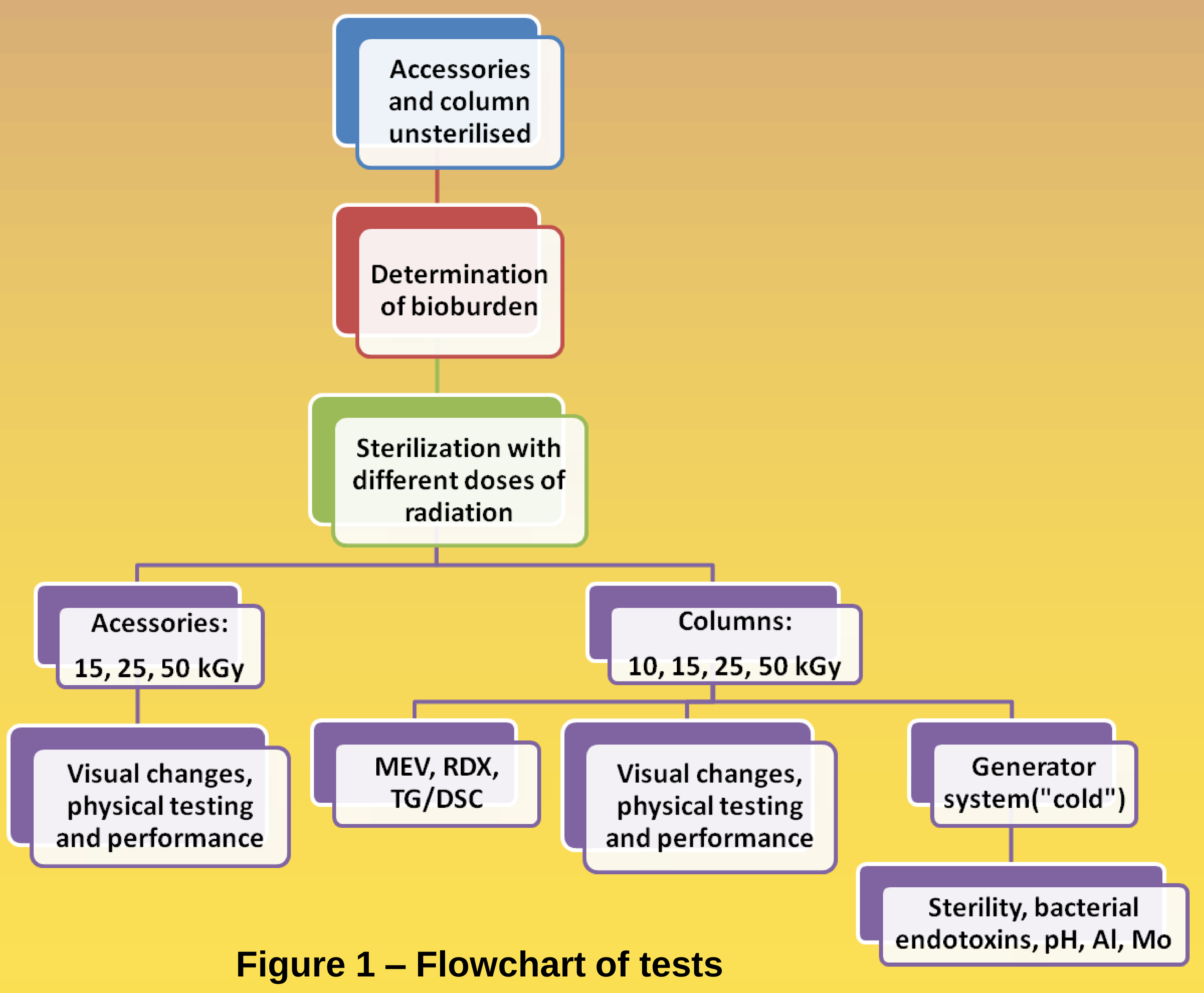

Figure 1 – Flowchart of tests

RESULTS

The bioburden results for generator accessories showed higher contamination levels in the generator lids with filter (390 colony forming units, CFU), in the top bungholes with Teflon® (190 CFU) and in the generator washing system (160 CFU). From the results obtained, the verification dose was estimated in approximately 10 kGy for all generator accessories and the sterilization dose (10^{-6} reduction) was 25 kGy.

The bioburden results for three different lots of columns were 2.3; 3.5; and 53 CFU, resulting in a verification dose (10^{-2} reduction) of approximately 7.2 kGy, and sterilization dose (s = 10^{-6}) of 20.3 kGy. The 10, 15, 25 and 50 kGy absorbed doses caused darkening of the glass column (Figure 2). This phenomenon was due to defects or imperfections caused by the exposure to radiation, which changed the color centers in the glass structure and caused the appearance of a brownish color.

The SEM images showed that the Al_2O_3 appeared fragmented at higher absorbed doses, especially 25 and 50 kGy. All elemental analysis spectra showed the predominance of aluminum and oxygen elements, as expected. Elemental analysis spectra (EDS) and X-ray diffraction showed no significant change in crystal structure of alumina subjected to different absorbed doses, because it is presented as the stable alpha structure (α-Al_2O_3). Teflon® had more significant changes in TG and DSC spectra for 25 and 50 kGy doses.

The performance tests in non-radioactive generator systems (Figure 3) showed increased presence of aluminum in the eluates of columns irradiated with lower absorbed doses whilst in all cases the MoO_4^{-2} adsorption yield was above 99.97%.

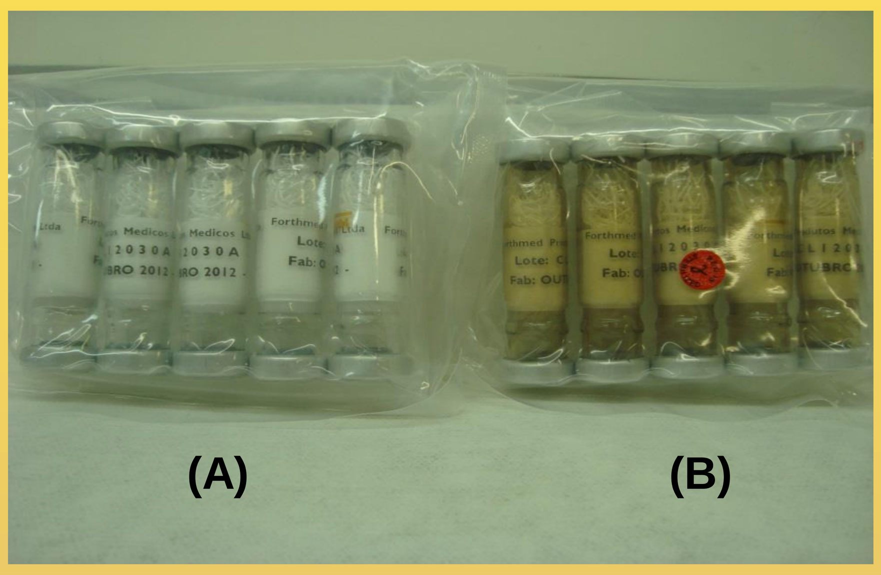

Figure 2 – Non-irradiated (A) and irradiated (B) glass columns with different absorbed doses

Figure 3 - Non-radioactive generator systems

CONCLUSION

Despite some alteration in the appearance and in the structure of the generator column materials, the elution performance remained practically unchanged showing that the sterilization of columns with ^{60}Co gamma radiation is feasible from a technical and economic point of view. Therefore, the most appropriate absorbed dose was 25 kGy based on the bioburden results and radiation effects on materials.