RADIATION STERILIZATION AND ITS CONSEQUENCE ON THE API

Radiation Sterilization (11)

The sterilization effect of the radiation rests on their biological effect.

When an ionizing radiation interacts with the matter, it releases an electron of their orbit that acquires a certain kinetic energy. The target atom loses an electron and becomes a positive ion. As for the released electrons, they strike other electrons on their pathway and are responsible for the formation of many other ions. In fact, the major part of ionizations is due to electrons whatever the incident radiation type may be (electron beam, γ or X ray).

The most critical damage caused by the ionizing radiations is made on the DNA molecule. The modifications of this macromolecule generate defects of genetic coding at the origin of changes or cellular death.

Actually, there are two processes of deterioration of the DNA molecule by the ionizing rays: either directly by ionization of the molecule and release of electrons as explained previously or by water radiolysis present in the microorganism's cell. This second phenomenon creates in the vicinity of the DNA molecule, powerful oxygen chemical reagents H_2O_2 or free radicals such as OH, H, HO_2, which will deteriorate the genetic material.

The ionizing rays deteriorate the vital structures of the living microorganisms whose consequences are generally lethal for them.

The inactivation of the microorganisms follows an exponential law and consequently there always exists a certain statistical probability that a microorganism can survive sterilization. The European and U.S. Pharmacopeia give a threshold value known as sterility assurance level (SAL) to reach so that sterilization is effective. Thus, the SAL for a given process is expressed like the probability of occurrence of a nonsterile article in a population of sterilized objects. For sterilization of drugs or medical devices, the SAL is set to 10^{-6} (4).

When using a radiation sterilization method, it is necessary to establish the dose received by the product to achieve sterility. The effectiveness of this dose must be shown and controlled over time. It thus requires validating the process that is the guarantee of the conformity of the product to the requirements retained by the legislation (3).

European Pharmacopeia indicates that the sterilization absorbed dose of reference is 25 kGy.[a] It also states that other values can be selected provided that they make it possible to obtain a SAL lower than 10^{-6}.

In the medical device industry, the validation of a radiation sterilization process is done on the ISO 11137 standard basis: *ISO standard 11137-2: 2006, Sterilization of health care products—Radiation—Part 2: Establishing the sterilization dose.* This text specifies methods to determine the minimum dose necessary to reach a specified requirement for sterility and methods to justify the use of the sterilization dose of 25 kGy or the sterilization dose of 15 kGy, to obtain a sterility insurance level of 10^{-6}.

[a] *Absorbed dose* is the mean energy imparted to a quantity of matter divided by the mass of that matter, i.e., energy per unit mass. Its unit is Gray (Gy). 1 Gy = 1 J/kg.