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Sterilization is defined as any process that effectively kills or eliminates almost all microorganisms like fungi, bacteria, viruses, spore forms. There are many different sterilization methods depending on the purpose of the sterilization and the material that will be sterilized. The choice of the sterilization method alters depending on materials and devices for giving no harm. These sterilization methods are mainly: dry heat sterilization, pressured vapor sterilization, ethylene oxide (EtO) sterilization, formaldehyde sterilization, gas plasma ($H_2O_2$) sterilization, peracetic acid sterilization, e-beam sterilization and gamma sterilization.

Gamma radiation sterilization and e-beam sterilization are mainly used for the sterilization of pharmaceuticals. Gamma radiation delivers a certain dose that can take time for a period of time from minutes to hours depending on the thickness and the volume of the product. E-beam irradiation can give the same dose in a few seconds but it can only give it to small products. Depending on their different mechanism of actions, these sterilization methods affect the pharmaceutical formulations in different ways. Thus, the sterilization method chosen must be compatible with the item to be sterilized to avoid damage.

To be effective, gamma or e-beam sterilization requires time, contact and temperature. The effectiveness of any method of sterilization is also dependent upon four other factors like the type of microorganism present. Some microorganisms are very difficult to kill. Others die easily the number of microorganisms present. It is much easier to kill one organism than many the amount and type of organic material that protects the microorganisms. Blood or tissue remaining on poorly cleaned instruments acts as a shield to microorganisms during the sterilization process, the number of cracks and crevices on an instrument that might harbor microorganisms. Microorganisms collect in, and are protected by, scratches, cracks and crevices such as the serrated jaws of tissue forceps.

Finally, here is no single sterilization process for all the pharmaceuticals and medical devices. It is hard to assess a perfect sterilization method because every method has some advantages and disadvantages. For this reason, sterilization process should be selected according to the chemical and physical properties of the product. It is fairly clear that different sterilization processes are used in hospital and in industry applications. While EtO or autoclave sterilization is used in hospitals, gamma radiation or e-beam sterilization is used in industry depending on the necessity of a developed institution. Superiority of radiation sterilization to EtO and other sterilization methods are known by all over the
world. These factors facilitate to understand the relatively fast increase of the constitution of irradiation institutions. Thus, this chapter will discuss the use of sterilization by gamma radiation.

2. Radiation processing

Radiation processing refers to the use of radiation to change the properties of materials on an industrial scale. The term ‘ionizing radiation’ relates to all radiation capable of producing ionization cascades in matter. The energy range characteristic of ionizing radiation begins at about 1000 eV and reaches its upper limit at about 30 MeV. To avoid induced radioactivity, which may appear if the gamma ray energy is higher than 5 MeV or the energy of the fast electrons exceeds 10 MeV, it is prohibited to use for sterilization radiation characterized by energy higher than these values. On the other hand, the application of lower energy radiation (below 0.2 MeV) is not rational. Commercial gamma ray irradiation facilities are typically loaded with $^{60}$Co of total activity from 0.3 to 3.0 MCI, while commercial e-beam facilities are equipped with one or two electron accelerators generating high power (10–100 kW) beams of 8–10 MeV electrons.

When radiation passes through materials it breaks chemical bonds. Radiation processing has been used commercially for almost forty years. Gamma radiation from $^{60}$Co, electron beams and x-rays, are all used to sterilize the medical devices used in operations and other healthcare treatments. Implants, artificial joints, syringes, blood-bags, gowns, bottle teats for premature baby units and dressings are all sterilized using radiation. The surgical gloves are sterilized using gamma radiation from $^{60}$Co. Other industries that benefit from radiation processing include the food, pharmaceutical, cosmetic, horticultural, and automotive industries. In the horticultural industry, growing-mats, fleeces and pots may be reused after irradiation-reducing waste and cost and saving the environment from unnecessary waste. Similarly, commercial egg trays may be recycled after irradiation without risk of proliferating salmonella.

Gamma rays are formed with the self disintegration of Cobalt-60 ($^{60}$Co) or Cesium-137 ($^{137}$Cs) sources. Among thousands of gamma emitters only $^{137}$Cs and $^{60}$Co are indicated for radiation processing. The energy of gamma rays, as electromagnetic quantum waves, is similar to light, but with higher photon energy and shorter wavelength. The $^{60}$Co radionuclide can be produced in a nuclear power reactor by the irradiation of $^{59}$Co (metal), with fast neutrons. The radioactive isotope is formed by neutron capture as showed equation 1 (Laughlin, 1989).

$$^{27}$Co$^{59} + ^0$n$^1 \rightarrow ^{27}$Co$^{60}$$

(1)

The unstable nucleus of $^{60}$Co emits photons of 1.17 and 1.33 MeV, decaying with a half-life of 5.2714 years to stable $^{60}$Ni as shown the Figure 1 (Kaplan, 1955). The radioactive $^{60}$Co source is composed of small pellets of cobalt that are loaded into stainless steel or zirconium alloy sealed tubes (pencil arrays).

Radiation is the unique source of energy which can initiate chemical reactions at any temperature, including ambient, under any pressure, in any phase (gas, liquid or solid),

\[ 1 \text{ Ci (currie)} = 3.7 \times 10^{10} \text{ Bq (becquerel)} \]
without use of catalysts. Thus, radiation processing uses highly penetrating gamma radiation from sealed radiation sources travelling at almost the speed of light, to bombard and kill bacteria in products sealed inside their final packaging. In this way the irradiated product remains sterile until the packaging is removed. The energy carried by the gamma radiation is transferred to the product being irradiated by collisions between the radiation and the atoms of the product. In these collisions atoms lose their bound electrons in a process called ionization. It is this process that results in irreparable damage to the life sustaining chemistry of living organisms and the initiation of crosslinking chemistry or main chain scission in polymeric materials.

![Disintegration of $^{60}$Co](image)

**Fig. 1. Disintegration of $^{60}$Co**

### 3. Gamma sterilization

#### 3.1 General aspects

Gamma rays are generally used for the sterilization of gaseous, liquid, solid materials, homogeneous and heterogeneous systems and medical devices, such as syringes, needles, cannulas, etc. Gamma irradiation is a physical means of decontamination, because it kills bacteria by breaking down bacterial DNA, inhibiting bacterial division. Energy of gamma rays passes through hive equipment, disrupting the pathogens that cause contamination. These photon-induced changes at the molecular level cause the death of contaminating organisms or render such organisms incapable of reproduction. The gamma irradiation process does not create residuals or impart radioactivity in the processed hive equipment. Complete penetration can be achieved depending on the thickness of the material. It supplies energy saving and it needs no chemical or heat dependence. Depending on the radiation protection rules, the main radioactive source has to be shielded for the safety of the operators. Storage of is needed depending on emitting gamma rays continuously

The first aspect to consider when sterilizing with gamma is product tolerance to the radiation. During use of this type of radiation, high-energy photons bombard the product,
causing electron displacement within. These reactions, in turn, generate free radicals, which aid in breaking chemical bonds. Disrupting microbial DNA renders any organisms that survive the process nonviable or unable.

Gamma radiation does have some significant advantages over other methods of producing sterile product. These benefits include: better assurance of product sterility than filtration and aseptic processing; no residue like EtO leaves behind; more penetrating than E-beam; low-temperature process and simple validation process.

Process validation may be defined as the documented procedure for obtaining, recording and interpreting the results required to establish that a process will consistently yield product complying with a predetermined specification. For sterilization, process validation is essential, since sterilization is one of those special processes for which efficacy cannot be verified by retrospective inspection and testing of the product. Process validation consists of: i. installation qualification of the facility; ii. operational qualification of the facility and iii. performance qualification of the facility (ISO 14937, 2000).

Radiation sterilization of medical products also is currently regulated by two standards, EN 552 (1994) and ISO 11137 (1995). These standards will be harmonized in the very near future into ISO 11137 (2006) part 1, part 2 and part 3. Currently, all three parts of ISO 11137 (2006) are at the Final Draft International Standard Stage (FDIS). These three documents are now published. All sterilization standards consider ‘dose’ as a key parameter in order to determine if a product is sterile. However, measurement of dose is not a trivial task and a commercial dosimetry system consists of dosimeters, readout equipment and procedure for its use. Dosimeters may be films, small plastic blocks, fluids or pellets where there is a known and reproducible response to radiation dose. The dosimetry system must be calibrated, and the calibration must be traceable to a national standard. ISO/ASTM standard 51261 gives guidelines for calibration procedures.

3.2 Effects of gamma rays on living organisms

Radiation effects on living organisms are mainly associated with the chemical changes but are also dependent on physical and physiological factors. Dose rate, dose distribution, radiation quality are the physical parameters. The most important physiological and environmental parameters are temperature, moisture content and oxygen concentration. The action of radiation on living organisms can be divided into direct and indirect effects. Normally, the indirect effects occur as an important part of the total action of radiation on it. The Figure 2 shown that radiolytic products of water are mainly formed by indirect action on water molecules yielding radicals \( \text{OH}^\cdot \), \( \text{e}^- \text{aq} \) and \( \text{H}^\cdot \). The action of the hydroxyl radical (OH•) must be responsible for an important part of the indirect effects. Drying or freezing of living organisms can reduce these indirect effects. If we consider pure water, each 100 eV of energy absorbed will generate: 2.7 radicals OH•, 2.6 e- aq, 0.6 radicals H•, 0.45 H₂ molecules and 0.7 molecules H₂O₂. (Borrely et al, 1998).

Several types of microorganism, mainly bacteria and, less frequently, moulds and yeasts, have been found on many medical devices and pharmaceuticals (Takehisa et al, 1998). Complete eradication of these microorganisms (sterilization) is essential to the safety of medical devices and pharmaceutical products. The sterilization process must be validated to verify that it effectively and reliably kills any microorganisms that may be present on the
Sterilization by Gamma Irradiation

pre-sterilized product. Radiation sterilization, as a physical cold process, has been widely used in many developed and developing countries for the sterilization of health care products. Earlier, a minimum dose of 25 kGy was routinely applied for many medical devices, pharmaceutical products and biological tissues. Now, as recommended by the International Organization for Standardization (ISO), the sterilization dose must be set for each type of product depending on its bioburden. Generally, the determination of sterilization dose is the responsibility of the principal manufacturer of the medical product, who must have access to a well qualified microbiology laboratory.

Fig. 2. Effect of gamma rays on water molecules

The lethal effect of ionizing radiation on microorganisms, as measured by the loss by cells of colony-forming ability in nutrient medium, has been the subject of detailed study. Much progress has been made towards identification of the mechanism of inactivation, but there still remains considerable doubt as to the nature of the critical lesions involved, although it seems certain that lethality is primarily the consequence of genetic damage. Many hypotheses have been proposed and tested regarding the mechanism of cell damage by radiation. Some scientists proposed the mechanism thought 'radiotoxins' that are the toxic substances produced in the irradiated cells responsible for lethal effect. Others proposed that radiation was directly damaging the cellular membranes. In addition, radiation effects on enzymes or on energy metabolism were postulated. The effect on the cytoplasmic membrane appears to play an additional role in some circumstances (Greez et al, 1983).

It is now universally accepted that the deoxyribonucleic acid (DNA) in the chromosomes represents the most critical ‘target’ for ionizing radiation because it is responsible for inhibition of cell division.

A DNA strand is composed of a series of nucleotides containing a purine (adenine, guanine) or a pyrimidine base (cytosine, thymine), a sugar (deoxyribose) bond to the base and a phosphate connected to the sugar. The nucleotides are joined by phosphodiester bonds
between the sugar and the phosphate. DNA is composed of two complementary anti-
parallel strands linked by hydrogen bonds between the bases. Thymine is complementary to
adenine (two hydrogen bonds between them) whilst guanine is the complementary base to
cytosine (linked by three hydrogen bonds). In the most frequent configuration, called B
form, the two strands are twisted to form a right-handed double helix. Ionizing radiation
can affect DNA either directly, by energy deposition in this critical target, or indirectly, by
the interaction of radiation with other atoms or molecules in the cell or surrounding the cell
like water. In particular, radiation interacts with water, leading to the formation of free
radiicals (see Figure 2) that can diffuse far enough to reach and damage DNA. It is worth
mentioning that the OH• radical is most important; these radicals formed in the hydration
layer around the DNA molecule are responsible for 90% of DNA damage. Consequently, in
a living cell, the indirect effect is especially significant. In a general sense, the death of a
microorganism is a consequence of the ionizing action of the high energy radiation. It is
estimated that the irradiation of a living cell at one gray induces 1000 single strand breaks,
40 double strand breaks, 150 cross-links between DNA and proteins and 250 oxidations of
thymine (ABCRI, 1992; Borrely et al, 1998).

Both prokaryotes (bacteria) and eukaryotes (moulds and yeasts) are capable of repairing
many of the different DNA breaks (fractures). Living organisms have developed different
strategies to recover from losses of genetic information caused by DNA damages. Damages
to DNA alter its spatial configuration so that they can be detected by the cell. In the case of
single strand breaks (Figure 3), the damaged DNA strand is excised and its complementary
strand is used to restore it. Efficient and accurate repair of the damages can take place as
long as the integrity of the complementary strand is maintained. Radiosensitivity is highly
influenced by the capability of the strain to repair single-strand breaks. Strains that lack this
ability are far more radiosensitive than the others (Tubiana et al., 1990; WHO, 1999). Double
strand breaks are far more hazardous since they can lead to genome rearrangements. Two
distinct mechanisms have been described for the repair of double strand breaks: non
homologous end joining and recombination repair (Broomfield et al., 2001).

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distinct mechanisms have been described for the repair of double strand breaks: non
homologous end joining and recombination repair (Broomfield et al., 2001).
ionization or to the indirect action of the radiolysis products of water, or both. However, while the work on basic mechanisms continues, much is already known both qualitatively and quantitatively in relation to the radiation inactivation of microbial populations. Just as with heat resistance, there is considerable variability in radiation resistance between microbial species; in general, viruses are more radiation resistant than bacterial spores, which in turn are more resistant than vegetative organisms, yeasts and moulds. Moreover, the inactivation of microbial populations is considerably influenced by conditions of environment during irradiation-for example, gaseous composition, temperature, and nature of the suspending medium.

Fig. 4. Combinational repair of DNA double break

3.2.1 Decimal reduction dose

When a suspension of a microorganism is irradiated at incremental doses, the number of surviving cell forming colonies after each incremental dose may be used to construct a dose survival curve, as shown in Figure 5. The radiation resistance of a microorganism is measured by the so-called decimal reduction dose (D$_{10}$ value), which is defined as the radiation dose (kGy) required to reduce the number of that microorganism by 10-fold (one log cycle) or required to kill 90% of the total number (Whitby & Gelda, 1979). The D$_{10}$ value

Fig. 5. Typical survival curve for a homogeneous microbial population.
Gamma Radiation

can be measured graphically from the survival curve, as shown in Figure 5; the slope of the curve (mostly a straight line) is related to the \( D_{10} \) value. With certain microorganisms, a ‘shoulder’ may appear in the low dose range before the linear slope starts. This ‘shoulder’ may be explained by multiple targets and/or certain repair processes being operative at low doses.

The decimal reduction dose is affected by irradiation conditions in which the microorganisms exist in dry or freezing, aerobic or anaerobic conditions. The \( D_{10} \) value of some organisms (responsible for selected water-born diseases) irradiated in buffer solution is presented in Table 1.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>( D_{10} ) (kGy)</th>
<th>Disease</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Salmonella typhimurium</em></td>
<td>0.30</td>
<td>Gastroenteritis</td>
<td>Borrely, 1998</td>
</tr>
<tr>
<td><em>Mycobacterium tuberculosis</em></td>
<td>0.30</td>
<td>Tuberculosis</td>
<td>IAEA, 1975</td>
</tr>
<tr>
<td><em>Shigella dysenteriae</em></td>
<td>0.60</td>
<td>Dysentery</td>
<td>IAEA, 1975</td>
</tr>
<tr>
<td><em>Vibrio cholerae</em></td>
<td>0.48</td>
<td>Cholera</td>
<td>IAEA, 1975</td>
</tr>
</tbody>
</table>

Table 1. Decimal reduction dose (\( D_{10} \)) of some microorganisms

There are many factors affecting the resistance of microorganisms to ionizing radiation, thus influencing the shape of the survival curve. The most important factors are:

a. Size and structural arrangement of DNA in the microbial cell;

b. Compounds associated with the DNA in the cell, such as basic peptides, nucleoproteins, RNA, lipids, lipoproteins and metal ions. In different species of microorganisms, these substances may influence the indirect effects of radiation differently;

c. Oxygen: The presence of oxygen during the irradiation process increases the lethal effect on microorganisms. Under completely anaerobic conditions, the \( D_{10} \) value of some vegetative bacteria increases by a factor of 2.5–4.7, in comparison with aerobic conditions;

d. Water content: Microorganisms are most resistant when irradiated in dry conditions. This is mainly due to the low number or absence of free radicals formed from water molecules by radiation, and thus the level of indirect effect on DNA is low or absent;

e. Temperature: Treatment at elevated temperature, generally in the sub-lethal range above 45°C, synergistically enhances the bactericidal effects of ionizing radiation on vegetative cells. Vegetative microorganisms are considerably more resistant to radiation at subfreezing temperatures than at ambient temperatures. This is attributed to a decrease in water activity at subfreezing temperatures. In the frozen state, moreover, the diffusion of radicals is very much restricted;

f. Medium: The composition of the medium surrounding the microorganism plays an important role in the microbiological effects. \( D_{10} \) values for certain microorganisms can differ considerably in different media;

g. Post-irradiation conditions: Microorganisms that survive irradiation treatment will probably be more sensitive to environmental conditions (temperature, pH, nutrients, inhibitors, etc.) than the untreated cells.

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In addition, it has been suggested that some pigments synthesized by microorganisms may play a role in their resistance towards ionizing radiation. For example, carotenoids synthesized by *Exiguobacterium acedicum* were found to be responsible for its radioresistance (Kim et al., 2007). Fungi that synthesize pigments such as *Curvularia geniculata* (melanin) or other *Dematiaceous fungi* that contain melanin and carotenoids have higher D$_{10}$ values (Saleh et al., 1988; Geis & Szaniszlo, 1984). These pigments appear to be involved in both photo- and radio-protection. It was also discovered that a higher amount of Mn$^{+2}$ in some radioreistant bacteria may partly explain their resistance due to the decrease of protein oxidation in presence of higher concentrations of Mn$^{+2}$ (Daly et al., 2007).

3.2.2 Sterilization dose

It can be defined as the absorbed energy per unit mass ([J.kg$^{-1}$] = [Gy]). Survival fraction of the microorganisms is reversely proportional with the absorbed dose. Doses for sterilization should be chosen according to the initial bioburden, sterility assurance level (SAL) and the radiosensitivity of microorganisms. A sterility assurance level (SAL) is derived mathematically and it defines the probability of a viable microorganism being present on an individual product unit after sterilization. SAL is normally expressed as 10$^{-n}$. SAL is generally set at the level of 10$^{-6}$ microorganisms/ml or g for the injectable pharmaceuticals, ophtalmic ointment and ophtalmic drops and is 10$^{-3}$ for some products like gloves that are used in the aseptical conditions. Generally for an effectively (F-value) of n = 8 is employed for sterilization of *Bacillus pumilus* for the standard dose of 25 kGy is equivalent to about eight times its D$_{10}$ (2.2-3 kGy).

The process of determining the sterilization dose is intended to establish the minimum dose necessary to achieve the required or desired sterility assurance level (SAL). Sterilization dose depends on: i. level of viable microorganisms on the product before the sterilization process (natural bioburden); ii. relative mix of various microorganisms with different D$_{10}$ values; iii. degree of sterility, i.e. sterility assurance level (SAL), required for that product. Because of this reason, the optimum sterilization dose is 25 kGy at the above level of bioburden (Takehisa et al., 1998).

On the other hand, the response of a microbial cell and hence its resistance to ionizing radiation depends of many factors like: i. nature and amount of direct damage produced within its vital target; ii. number, nature and longevity of radiation induced reactive chemical changes; iii. inherent ability of the cell to tolerate or correctly repair the damage and iv. influence of intra and extracellular environment on any of the above.

In general, bioburden on any product is made up of a mixture of various microbial species, each having its own unique D$_{10}$ value, depending on its resistance to radiation; these various species exist in different proportions. A standard distribution of resistances (D$_{10}$ values) has been agreed upon for the determination of sterilization dose based on Method 1 of ISO 11137 (1995). Thus, 65.487% of the microorganisms on a product has a D$_{10}$ value of 1.0 kGy, 22.493% of the microorganisms has a D$_{10}$ value of 1.5 kGy, etc. This is an average distribution based on significant amounts of data. It is not always that this distribution exists; it would depend on the conditions of manufacturing and subsequent processes. Method 1 of ISO 11137 (1995) is based on confirming that this distribution exists. From the reported survival data resulting from numerous investigations carried out on the effects of ionizing radiation on microorganisms, the following observations may be made:
1. Generally, bacterial spores are considered more radiation resistant than vegetative bacteria;
2. Among vegetative bacteria, gram-positive bacteria are more resistant than gram-negative bacteria;
3. Vegetative cocci are more resistant than vegetative bacilli;
4. Radiation sensitivity of moulds is of the same order as that of vegetative bacteria;
5. Yeasts are more resistant to radiation than moulds and vegetative bacteria;
6. Anaerobic and toxigenic Clostridium spores are more radiation resistant than the aerobic non-pathogenic Bacillus spores;
7. Radiation resistance of viruses is much higher than that of bacteria or even bacterial spores;
8. The majority of fungi have $D_{10}$ values between 100-500 Gy. Dematiaceous fungi, which are found in soils and rotten woods but normally not in pharmaceuticals, are highly radioresistant with $D_{10}$ values from 6 to 17 kGy. Yeast is more resistant than other fungi. Candida albicans for example was found to be quite radioresistant with $D_{10}$ of 1.1 to 2.3 kGy;
9. In general, it is observed that viruses are less sensitive towards ionizing radiation than bacteria and fungi. $D_{10}$ values for most viruses range from 3 to 5 kGy (Grieb et al., 2005), which is far more than bacteria. Radiation sensitivities of single stranded DNA viruses are higher than those of double stranded ones;
10. Viruses should not normally be found in pharmaceuticals, except in those originating from biotechnological processes. Biological products are submitted to specific guidelines (IAEA, 2004) and the use of higher irradiation doses may be validated for the elimination of viruses. Inactivation with a sufficient S.A.L. ($<10^{-9}$) of viruses such as HIV or hepatitis in grafts necessitates high doses from 60 to 100 kGy (Campbell & Li, 1999). Table 2 showed the radiosensivities of some microorganisms at determined conditions.

3.2.3 Effect of temperature and additive on radiosensitivity of living organisms

Temperature plays a major role in the radiosensitivity of microorganisms. As temperature decreases, water radicals become less mobile. As a general rule, microorganisms are less radioresistant when irradiated at low temperatures (Thayer & Boyd, 2001). For example, whilst sensitivity of spores from Bacillus megaterium was constant between -268 and -148°C, an increase in temperature to 20°C led to a 40% increase in sensitivity. Effect of temperature was observed to be similar for oxic and anoxic spores (Helfinstine et al., 2005).

The indirect effect is partially abolished by freezing the solution. The highest decrease in sensitivity is observed between 0 and -15°C. For example, $D_{10}$ value of Escherichia coli irradiated in meat increased from 0.41 kGy at +5°C to 0.62 kGy at -15°C. For Staphylococcus aureus, $D_{10}$ at -76°C was 0.82 kGy instead of 0.48 kGy at +4°C (Sommers et al., 2002). Subfreezing temperatures offer less protection for spores than for vegetative species since they already have low moisture content. The irradiation of frozen aqueous solutions allowed minimizing the loss of active substance even for a 25 kGy dose. This approach seems to be the most promising method for terminal sterilization of aqueous solutions by ionizing radiations. The major radiolysis product was formed after the attack of the electron. Some of the radiolysis products detected were attributed to the attack of $^\bullet$OH,
Table 2. Radiosensivities of some microorganisms

<table>
<thead>
<tr>
<th>organism</th>
<th>classification</th>
<th>D_{10} (kGy)</th>
<th>condition</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clostridium botulinum spores</td>
<td>bacteria</td>
<td>2.9</td>
<td>0°C, Phosphate Buffer</td>
<td>Grecz et al., 1965</td>
</tr>
<tr>
<td>Clostridium botulinum spores</td>
<td>bacteria</td>
<td>4.6</td>
<td>Meat, 0°C</td>
<td>Grecz et al., 1965</td>
</tr>
<tr>
<td>Clostridium botulinum spores</td>
<td>bacteria</td>
<td>3.9</td>
<td>Phosphate Buffer, -196°C</td>
<td>Grecz et al., 1965</td>
</tr>
<tr>
<td>Clostridium botulinum spores</td>
<td>bacteria</td>
<td>6.8</td>
<td>Meat, -196°C</td>
<td>Grecz et al., 1965</td>
</tr>
<tr>
<td>Aspergillus flavus</td>
<td>fungi</td>
<td>0.60</td>
<td>Aerated water, 20°C</td>
<td>Saleh et al., 1988</td>
</tr>
<tr>
<td>Aspergillus niger</td>
<td>fungi</td>
<td>0.42</td>
<td>Aerated water, 20°C</td>
<td>Saleh et al., 1988</td>
</tr>
<tr>
<td>Cladosporium cladosporioides</td>
<td>fungi</td>
<td>0.03-0.25</td>
<td>Aerated water, 20°C</td>
<td>Saleh et al., 1988</td>
</tr>
<tr>
<td>Curvularia geniculata</td>
<td>fungi</td>
<td>2.42-2.90</td>
<td>Aerated water, 20°C</td>
<td>Saleh et al., 1988</td>
</tr>
<tr>
<td>Coxsackievirus B-2</td>
<td>viruses</td>
<td>5.3</td>
<td>Water, -90°C</td>
<td>Sullivan et al., 1973</td>
</tr>
<tr>
<td>Coxsackievirus B-2</td>
<td>viruses</td>
<td>7.0</td>
<td>Meat, 16°C</td>
<td>Sullivan et al., 1973</td>
</tr>
<tr>
<td>Coxsackievirus B-2</td>
<td>viruses</td>
<td>8.1</td>
<td>Meat, -90°C</td>
<td>Sullivan et al., 1973</td>
</tr>
<tr>
<td>HIV</td>
<td>viruses</td>
<td>8.8</td>
<td>Bone, -78°C</td>
<td>Campbell and Li, 1999</td>
</tr>
</tbody>
</table>

demonstrating the feasibility of a reaction between the •OH from ice radiolysis and the solute. A comparison was performed with irradiated frozen solutions of metoprolol, which has been studied in liquid aqueous solutions (Crucq et al, 2000). Degradation of metoprolol when irradiated in frozen solutions was negligible.

On the other hand, the evaluation of the radiosensitivity of bacteria as a function of the addition of radical scavengers is quite difficult since many experiments have been carried out either on isolated DNA, which does not take into account the effects within the cell. For experiments carried out on bacteria, the concentration of the scavenger within the cell was assumed to be equal to that of the extracellular media, which is generally not the case.

It was shown that the protection of bacteria against ionizing radiation in the presence of hydroxyl radical scavengers was highly dependent of the irradiation conditions (Billen, 1984). Scavengers are unable to prevent semi-direct effect due to the hydroxyl radicals from the bound water since the water lattice around DNA does not possess any solvent power (Korystov, 1992). Therefore, scavenging of the radicals from the bound water by an exogenous protector is almost impossible. It was observed that thiols are able to repair DNA damaged sites before a breakage occurs (ABCRI, 2001).
4. Gamma sterilization of human tissue grafts

Connective tissue allografts, such as bone, cartilage, tendons, ligaments, dura mater, skin, amnion, pericardium, heart valves and corneas, are widely used for reconstructive surgery in many clinical disciplines, including orthopaedics, traumatology, neurosurgery, cardiosurgery, plastic surgery, laryngology and ophthalmology. The grafts are prepared by specialized laboratories called ‘tissue banks’. The risk of infectious disease transmission with tissue allografts is a major concern in tissue banking practice.

Microorganisms can be introduced into grafts during tissue procurement, processing, preservation and storage, but even if all these procedures are done under aseptic conditions, the possibility of bacterial, fungal and viral disease transmission of donor origin cannot be excluded. Bacterial, including tuberculosis, fungal, and viral infections, such as human immunodeficiency virus (HIV), hepatitis B and C (HBV, HCV), cytomegalovirus (CMV), as well as rabies and prion diseases, have been transmitted by tissue allografts. Thus, radiation sterilization of tissue grafts has been implemented in some tissue banks, and a dose of 25 kGy has been used in many of these tissue banks. The advantage of radiation sterilization is that it allows the processing of grafts, which have been previously sealed or tightly closed in special wrappings. Such procedures prevent any accidental recontamination during packing.

The problem is additionally complicated by the possible presence, in human tissues, of pathogenic viruses, such as the human immunodeficiency virus (HIV) (Daar et al, 1991), hepatitis viruses (HBV, HCV) (Conrad et al, 1995), cytomegalovirus or others. Data concerning the sensitivity of these viruses to ionizing radiation are scarce. This is mainly due to the fact that there are no suitable tests to study their inactivation, no appropriate animal models exist and no suitable method of in vitro culture of highly differentiated target cells (e.g. hepatocytes) for these viruses has yet been developed.

The wide range of $D_{10}$ values (4–8.3 kGy) determined for HIV and other viruses might be due to the influence of environmental conditions. Many factors can modify the sensitivity of pathogens microorganisms to ionizing radiation, including the temperature of irradiation. For example, the reduction of HIV virus was achieved with a dose of 50–100 kGy in frozen plasma (−80°C), and with 25 kGy at 15°C (Hiemstra et al, 1991). The $D_{10}$ value for HIV-1 irradiated at room temperature was 7.2 kGy, and 8.3 kGy at −80°C (Hernigou et al, 2000). The presence or absence of water and oxygen, and presence of radiation protectors are also factors can modify the sensibility of pathogens microorganisms. In the absence of water (for example, in dry air or lyophilized grafts) the resistance of pathogens increases. On the other hand, in the presence of water, an indirect effect of ionizing radiation predominates and the sensitivity of microorganisms increases. Oxygen enhances the damaging effect to microorganisms and further increases their sensitivity to radiation as discussed previously. Therefore, if lyophilization is used as a preservation procedure, it would be better to leave some amount of water in the tissue than attempt to remove as much water as possible. It should be noted that irradiation at low temperatures increases, while that at higher temperatures decreases the resistance of bacteria and viruses.
Collagen is a very variable protein, forming the basis of many connective and support tissues. It is a fibrous structural protein, with a distinctive structure. It has been postulated that polypeptide chain scissions (direct effect) predominate when collagen is irradiated in a dry state due to the direct effect of ionizing radiation, and this, in turn, dramatically increases collagen solubility in vitro and the rate of bone matrix resorption in vivo. It has been found, however, that a crosslinking reaction (indirect effect) appears during the irradiation of collagen in the presence of water (indirect effect), probably due to the action of highly reactive, short lived hydroxyl radicals (• OH) resulting from water radiolysis. The Figure 6 shown the simplified scheme illustrating the direct and indirect effects of gamma irradiation on bone molecules.

5. Gamma sterilization of food

Food sterilization by gamma irradiation is the process of exposing food to ionizing radiation to destroy microorganisms, bacteria, viruses, or insects that might be present in the food. Irradiated food does not become radioactive, but in some cases there may be subtle chemical changes.

The treatment of solid food by ionizing radiation can provide an effect similar to heat pasteurization of liquids, such as milk. The use of the term "cold pasteurization" to describe irradiated foods is controversial, since pasteurization and irradiation are fundamentally different processes. Food irradiation is currently permitted by over 50 countries, and the volume of food treated is estimated to exceed 500,000 metric tons annually worldwide. (Farkas & Farkas, 2011).
By irradiating food, depending on the dose, some or all of the harmful bacteria and other pathogens present are killed. This prolongs the shelf-life of the food in cases where microbial spoilage is the limiting factor. Some foods, e.g., herbs and spices, are irradiated at sufficient doses (5 kGy) to reduce the microbial counts by several orders of magnitude; such ingredients do not carry over spoilage or pathogen microorganisms into the final product. It has also been shown that irradiation can delay the ripening of fruits or the sprouting of vegetables. Insect pests can be sterilized (be made incapable of proliferation) using irradiation at relatively low doses. The use of low-level irradiation as an alternative treatment to pesticides for fruits and vegetables that are considered hosts to a number of insect pests, including fruit flies and seed weevils. The table 3 showed some use of food irradiation.

Exposure to gamma irradiation doses below 10 kGy is effective in enhancing food safety through the inactivation of pathogenic microorganisms such as *Salmonella* and *Campylobacter* and in extending the shelf-life of the diet by eliminating the microorganisms responsible for food spoilage. Irradiation doses of between 20 to 25 kGy and between 20 to 30 kGy are used most frequently to treat diets intended for specific pathogen-free animals, whereas larger doses of 40 to 50 kGy are recommended for diets intended for gnotobiotic or germ-free animals, where absolute sterility is essential.

<table>
<thead>
<tr>
<th>Type of food</th>
<th>Effect of Irradiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meat, poultry</td>
<td>Destroys pathogenic fish organisms, such as <em>Salmonella</em>, <em>Campylobacter</em> and <em>Trichinae</em></td>
</tr>
<tr>
<td>Perishable foods</td>
<td>Delays spoilage; retards mold growth; reduces number of microorganisms</td>
</tr>
<tr>
<td>Grain, fruit</td>
<td>Controls insect vegetables, infestation dehydrated fruit, spices and seasonings and reduces rehydration time</td>
</tr>
<tr>
<td>Onions, carrots, potatoes, garlic, ginger</td>
<td>Inhibits sprouting</td>
</tr>
<tr>
<td>Bananas, mangos, papayas, guavas, other non-citrus fruits</td>
<td>Delays ripening avocados, natural juices.</td>
</tr>
</tbody>
</table>

Table 3. Food irradiation use

The effects of irradiation on the nutritive value of a product must be established before sterilization by radiation can become an important method for preserving food. The irradiation produces no greater nutrient loss than what occurs in other processing methods. Sample of a rat diet in which the protein 5, 10, 25, 35 and 70 kGy, and the effects on protein quality are given in Table 4. The results indicate no significant effect of irradiation on protein quality. Amino acid composition was similarly very little affected (Ley, 1969). By comparison of the different treatments (different radiation doses) and the control sample (not irradiated) of bean, it was observed that there was no significant alteration in the amino acid contents up to the maximum dose of 10 kGy. Even the more sensitive amino acids, such as the aromatic and basic, under the effect of gamma rays were kept intact in the samples. These results indicate that it is possible to use irradiation to reduce grain losses using different radiation doses without causing significant changes in the amino acid contents.

On the other hand, irradiation reduces the vitamin content of food, the effect of which may be indirect in that inadequate amounts of antioxidant vitamins (such as C, E, and β-
carotene) may be available to counteract the effects of free radicals generated by normal cell metabolism. When food is irradiated, ionizing radiation reacts with water in the food, causing the release of electrons and the formation of highly reactive free radicals (see Figure 2). The free radicals interact with vitamins in ways that can alter and degrade their structure and/or activity (Murano, 1995). The extent to which vitamin loss occurs can vary based on a number of factors, including the type of food, temperature of irradiation, and availability of oxygen. Nonetheless, vitamin loss almost always increases with increasing doses of radiation. The destruction of vitamins continues beyond the time of irradiation. Therefore, when irradiated food is stored, it will experience greater vitamin loss than food that has not been irradiated. Cooking further accelerates vitamin destruction in irradiated food more than in non-irradiated food (Diehl, 1967).

**Table 4. Effect of gamma irradiation on the protein of rat diet**

<table>
<thead>
<tr>
<th>Dose (kGy)</th>
<th>True digestibility</th>
<th>Biological value</th>
<th>Net proteins utilization</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>85.6</td>
<td>80.5</td>
<td>68.9</td>
</tr>
<tr>
<td>5</td>
<td>83.6</td>
<td>75.8</td>
<td>63.5</td>
</tr>
<tr>
<td>10</td>
<td>86.5</td>
<td>81.7</td>
<td>70.6</td>
</tr>
<tr>
<td>25</td>
<td>87.0</td>
<td>78.1</td>
<td>68.0</td>
</tr>
<tr>
<td>35</td>
<td>84.8</td>
<td>77.3</td>
<td>65.4</td>
</tr>
<tr>
<td>70</td>
<td>85.3</td>
<td>76.4</td>
<td>65.2</td>
</tr>
</tbody>
</table>

Vitamin C, vitamin B1, and, vitamin E are reduced in foods exposed to commercial levels of irradiation (1 kGy - 4.5 kGy). At the low doses of 0.3 to 0.75 kGy, food irradiation has been found to destroy up to 11% of vitamin C in fruit before storage, and up to 79% of vitamin C after three weeks of storage (Mitchell et al, 1992). Additionally, at the limit of its shelf life (270 days) irradiated mango pulp contains 57% less vitamin C than non-irradiated mango pulp at the limit of its shelf life (60 days). Whole grains, beans, and meat are important sources of thiamine (vitamin B1), which helps convert carbohydrates into energy. It is essential for heart, muscle, and nervous system function. Wheat flour irradiated at the low dose of 0.25 kGy lost up to 20 percent of thiamine initially and 62% after three months of storage.25 Beef irradiated at 3.0 kGy, which is below the legal limit, experienced a 19 % loss of thiamine. Oils, corn, nuts, seeds, and green vegetables are important sources of vitamin E, an antioxidant that protects body tissues and cells. It also may improve the immune system and help fight heart disease, cancer, Alzheimer’s disease, and cataracts. Hazelnuts irradiated at 1.0 kGy lost 17% of vitamin E upon irradiation, and 58% of vitamin E after three months of storage and 30 minutes of baking. In addition, studies at higher levels of irradiation have demonstrated the destruction of vitamins A and K in food (Stevinson et al, 1959). The question of vitamin K in irradiated diets requires special considerations: i. it is known to be susceptible to destruction by y-irradiation (Ley, 1969); ii. it is synthesized by microbial action in the gut, and animals (particularly those that practice coprophagy) can satisfy part of their requirement by this means. Sterilized diets are usually only fed to specified-pathogen-free or gnotobiotic animals, i.e. those that have a limited gut microflora or none at all. Thus the organisms responsible for vitamin K synthesis are likely to be absent, and the animal's requirement for dietary vitamin K may be very much higher than that of its conventional counterpart. It is difficult, if not impossible to determine vitamin K chemically.
in animal diets because other components react as vitamin K to the assay procedure. Assessment of the vitamin K content of a diet must therefore depend on the response of the animals receiving it. The Table 5 gives the doses, which the some food vitamins lost.

<table>
<thead>
<tr>
<th>Food</th>
<th>Dose of sterilization (kGy)</th>
<th>Vitamins lost</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mango</td>
<td>10</td>
<td>Vitamin C</td>
<td>Youssef et al., 2002</td>
</tr>
<tr>
<td>Grapefruit</td>
<td>10</td>
<td>Vitamin C</td>
<td>Patil et al., 2004</td>
</tr>
<tr>
<td>Pork</td>
<td>10</td>
<td>Thiamin</td>
<td>Fox et al., 1997</td>
</tr>
<tr>
<td>Chicken</td>
<td>30</td>
<td>Vitamin E and Thiamin</td>
<td>Lakritz and Thayer, 1992</td>
</tr>
<tr>
<td>Beef</td>
<td>45</td>
<td>Thiamin</td>
<td>Fox et al., 1995</td>
</tr>
</tbody>
</table>

Table 5. Vitamins lost after gamma irradiation of some food

A study of the vitamin contents of diets for guinea-pigs (RGP), chicks (SCM) and cats after irradiation at doses ranging from 20 to 50 kGy has been made (Coates et al., 1969). At doses of the order of 20 to 30 kGy, vitamin losses from the guinea-pig and chick diets were very small indeed, but a severe loss of vitamin A from the cat diet was observed after treatment at 25 kGy. The losses were such that they could have been compensated for by addition of about twice the usual supplement of the vitamins affected. Stability decreased markedly with increased moisture content of the diet.

Poly unsaturated fatty acids were reported to have beneficial effects on human health and also are susceptible to peroxidation damage (Haghparast et al., 2010). Therefore, stability of these components needs to be considered for the standardization of the radiation process (Erkan and Özden, 2007). Ionizing radiation causes the radiolysis of water which is present to a great extent in food. This generates free radicals (see Figure 2) all of which react with the food constituents. The most susceptible site for free radical attack in a lipid molecule is adjacent to the double bonds. The most affected lipids during irradiation are thus the polyunsaturated fatty acids that bear two or more double bonds (Brewer, 2009).

Study on chicken showed no significant difference in total saturated and unsaturated fatty acids between irradiated (1, 3, 6 kGy) and non-irradiated frozen chicken muscle (Rady et al., 1988), however Katta et al. (1991) found significant decrease in the amount of palmitic acid and increase in oleic acid as irradiation dose level increased (0.5-3 kGy) in chicken meat.

Changes in the palmitic (C16:0), oleic (C18:1) and linoleic (C18:2) fatty acids of soybeans at different radiation doses (1, 5, 10, 20, 40, 60, 80 and 100 kGy) were no found (Hafez et al., 1985). The irradiation at 10 kGy also changes the linoleic and linolenic acid contents of grass prawns. Irradiation caused a 16% decrease in linoleic acid content, whereas linolenic acid was not affected significantly (Hau and Liew, 1993).

The irradiation of fish no changes fatty acid compositions of two species of Australian marine fish irradiated at doses of up to 6 kGy (Armstrong et al., 1994), but chemical components of tilapia and Spanish mackerel has been reported (Al- Kahtani et al., 1996). Irradiation of tilapia at 1.5–10 kGy caused a decrease in myristic (C14:0), palmitic (C16:0) and palmitoleic (C16:1) fatty acids. In the case of Spanish mackerel, palmitic (C16:0) and...
palmitoleic (C16:1) fatty acids decreased when irradiated at 1.5–10 kGy. Contents of total saturated fatty acids in the muscle of non-irradiated sea bream was respectively lower than in 2.5 kGy irradiated sea bream and higher than in 5 kGy irradiated sea bream. There was significant difference in the content of total unsaturated fatty acids, mono unsaturated fatty acids between 2.5 kGy and 5 kGy irradiated sea bream and no significant difference was determined in the content of unsaturated fatty acids, mono unsaturated fatty acids between non-irradiated and irradiated fish. On the other hand, the content of poly unsaturated fatty acids in the muscle of 5 kGy irradiated sea bream was significantly lower than in non-irradiated and 2.5 kGy irradiated sea bream (Erkan & Özden, 2007). All at same, the total saturated and total monounsaturated fatty acid contents were 27.97% and 24.72% for non-irradiated for sea bass, respectively. The amounts of these two fatty acids in irradiated samples increased to 28.18 and 25.75% for 2.5 kGy and 29.08 and 28.54% for 5 kGy. Significant difference also was found in the content of total unsaturated fatty acids, mono unsaturated fatty acids between 2.5 kGy (25.75%) and 5 kGy (28.54%) irradiated sea bass and between non-irradiated and irradiated fish. (Özden & Erkan, 2010).

Irradiated ground beef samples with 7 kGy had the highest total trans fatty acids, total monounsaturated and total unsaturated fatty acids than the other samples. Results showed an increase in trans fatty acids related to the increase on irradiation dose in ground beef and irradiation dose changed fatty acids composition especially trans fatty acids in ground beef (Yılmaz & Gecgel, 2007). Total saturated fatty acids and unsaturated fatty acids, mono unsaturated fatty acids of beef lipid increased with irradiation (1.13, 2.09 and 3.17 kGy), but ratios of unsaturated fatty acids, mono unsaturated fatty acids to saturated fatty acids did not change. Whilst, total poly unsaturated fatty acids reduced with irradiation, which resulted in poly unsaturated fatty acids to saturated fatty acids ratio decrease.

6. Gamma sterilization of medical devices

When radiation is used for the sterilization of medical devices, the compatibility of all of the components has to be considered. Ionizing radiation not only kills microorganisms but also affects material properties. Medical devices are made of many different materials, some of which are metals, but most are non-metals, such as formed polymers, composite structures and even ceramics. Radiation itself does not directly affect metals since sterilization energies are safely below any activation thresholds. Metals, such as those used in orthopaedic implants, are virtually unchanged by the radiation sterilization process. Nevertheless, it has to be kept in mind that some types of polymers when irradiated in contact with a metal can cause some corrosion of the metal or surface discoulouration. This is generally caused from by products released by some polymers during irradiation.

Polymer devices subjected to irradiation sterilization will inevitably be affected by the radiation and the environment used during sterilization, and will experience changes in the polymer structure such as chain scission and crosslinking (Schnabel, 1981). For some polymers both processes coexist and either one may be predominant depending not only upon the chemical structure of the polymer, but also upon the conditions of irradiation is performed like temperature, environment, dose rate, etc. The crosslinking and main scissions that take place during irradiation may lead to sharp changes in physical properties of the polymers. These effects will lead to changes in the tensile strength, elongation at break and impact strength. The exact changes seen will depend both on the basic polymer and any
Gamma Radiation

additives used. The changes in mechanical properties may not be immediately apparent and there can be some time delay in their development. One visible side effect of irradiation sterilization is that many plastics will discolor or yellow as a result of the processing. Irradiated devices are completely safe to handle and can be released and used immediately after sterilization.

Many polymers are resistant to radiation at doses of up to around 25 kGy, the actual doses used will be higher than this to achieve sterilization, however complete sterilization and radiation damage of some magnitude will inevitably occur. The effect of radiation is cumulative and for items that must be repeatedly sterilized the total dosage can rise rapidly. For these items records need to be kept to insure that safe limits are not exceeded. Irradiation is very effective for fully packaged and sealed single-use items where only one radiation dose is required.

6.1 Effects of gamma sterilization in polymeric medical device

Poly(vinyl chloride), PVC, is a polymer widely used for radiosterilizable food packaging and medical devices. However when the polymer systems are submitted to sterilization by gamma radiation (25 kGy dose), their molecular structures undergo modification mainly as a result of main chain scission and crosslinking effects. For PVC both processes coexist and either one may be predominant depending upon the conditions (temperature, environment, dose rate, etc.) under which irradiation is performed. The crosslinking and main scissions that take place during irradiation may lead to sharp changes in physical properties of the PVC (Vinhias et al, 2004).

During the interaction of gamma radiation with PVC, the reactions shown in Figure 7 can take place (Bacarro et al., 2003). This interaction gives rise to macroradicals deriving from C-Cl bond scission reactions (reaction I). The chlorine radical continues the reaction by way of a form center reaction in which HCl is formed and acts as a catalyst (reaction II). The A, B or C macroradicals recombine with each other forming networks due the restricted mobility of the macroradicals in the solid state (reaction III). It was reported, which crosslinking effect is predominant for PVC irradiated at lower doses (Silva et al, 2008). Oxidation reactions of macroradicals A, B or C (reaction IV), interaction of radical A with neighboring double bonds and other macroradicals from the impurities or from direct action of gamma radiation also can play an important role on crosslinking effect of PVC irradiated at lower radiation dose. However in presence of air the polymeric radicals A, B and C react with oxygen from air producing the peroxyl macroradical (reaction V). This radical formed can them undergo further reactions leading to main chain scission. This effect is predominant when the PVC molecule is irradiated at higher doses. Thus in the sterilization dose the commercial PVC undergoes the main chain scission (Ferreira et al, 2008).

Poly(methyl methacrylate), PMMA, also is used in manufacturing of medical supplies that can be sterilized by gamma irradiation at dose of 25 kGy and used in absorbed dose measurements in intense radiation fields. In general, polymer radicals are responsible for changes in the physical properties of PMMA. In particular, gamma irradiation of PMMA causes main scission and hydrogen abstraction from an α-methyl or methylene group. The extent of formation of each of the derivatives resulting from irradiation depends on the physical state of PMMA (Schnabel, 1981). The great majority of authors have reported that

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scission results from a macroradical that itself is radiolysis product of a lateral bond as shown in the Figure 8 (reaction I) (Guillet, 1985). The volatile products like HCOOCH₃, CO, CO₂, HCOCH₃ and CH₄ can be accounted for by the subsequent reactions of the carbomethoxy radical (B radical). The formation of C radical is the basic reason for the radiation-induced degradation of PMMA. Under air atmosphere the C radical undergoes the chain oxidation process forming the peroxyl free radical (D). Once D radical is formed in PMMA, it can abstract hydrogen from PMMA chains to form hydroperoxide. The hydroperoxide decomposes slowly but steadily at room temperature to generate new oxidative products, which induce further degradation. In addition, it is believed that the free radical A, peroxyl radical (B) and the hydroperoxides are the main substances, which induce the changes in PMMA properties when it is gamma irradiated (Schnabel, 1981).

Fig. 7. Effects of gamma irradiation on PVC molecule

Polycarbonate (PC) fills an important niche as one of the most popular engineering resins in the medical device market. Bisphenol-A polycarbonate has been commercially available since the 1960s, and its use in medical devices dates from approximately that time. Possessing a broad range of physical properties that enable it to replace glass or metal in many products, polycarbonate offers an unusual combination of strength, rigidity, and toughness that helps prevent potentially life-threatening material failures. In addition, it provides glasslike clarity, a critical characteristic for clinical and diagnostic a setting in which visibility of tissues, blood, and other fluids is required because biocompatibility is essential for any material used in direct or indirect contact with patients (Freitag et al., 1988).
Fig. 8. Radiolytic degradation of PMMA

The radiation-induced main chain scissions on PC occur in the carbonate groups, causing the evolution of carbon monoxide, carbon dioxide and hydrogen. The radiolysis of PC produces phenoxy and phenyl polymeric radicals that cause yellowness of the polymer. However, it has been reported in the literature that the crosslinking effect predominates at small doses, whereas at higher doses the main chain scission is more pronounced (Araujo et al, 1998).

Polyurethane (PU) is widely used in various medical devices because of its biocompatibility, and has some reports concerning its physicochemical stability and biological safety. However, among substances which were produced by degradation of PU, it was reported that a carcinogen, 4,4'-methylenedianiline (MDA), was produced from PU sterilized by gamma irradiation. On the other hand, a modified PU was produced and called thermosetting PU. In the case of thermosetting PU used in medical devices such as potting material in artificial dialysis devices, plasma separators, etc., the production of MDA upon sterilization showed a reverse tendency to non modified PU (Shintani, 1992). Their components and characteristics used in PU fabrication are much different, however their influences on the production of MDA by sterilization have not been sufficiently clarified.

As shown in Figure 9, it was suggested that the mechanism of MDA production might be the cleavage at urethane linkage successive to the terminalamino group, by radiation or hydrolysis (Shintani, 1992). Since more hydrophilic components were detected in the current experiment, we speculate the major cleavage portion will be at urethane linkage, thus producing MDA. The possibility of the cleavage at benzene-CH, linkage will not be significant due to no aniline or p-toluidine production.
Ultrahigh molecular weight polyethylene (UHMWPE) possesses a unique structure and properties which have resulted in its having been the most widely used material for replacing damaged or diseased cartilage in total joint replacements for the last 35 years. UHMWPE is a linear (non-branching) semi-crystalline polymer which can be described as a two-phase composite of crystalline and amorphous phases. The two resins of UHMWPE that are currently used in orthopaedics are GUR 1020 (3.5 million g/mol) and GUR 1050 (5.5–6 million g/mol). Orthopaedic components machined from UHMWPE are typically sterilized by irradiation with 25 kGy of $^{60}$Co gamma rays (Goldman et al, 1998). Such strong ionizing radiation is likely to have a detrimental effect upon the microstructure, such as entanglement density and tie molecules that give UHMWPE its needed properties for total joint replacement applications. The high-energy photons, such as gamma rays, can generate free radicals in polymers (P) through homolytic bond cleavage (reaction 1 in Figure 10). These radicals have been shown to have long lifetimes, especially those generated in the crystalline regions of the polymer where they can diffuse at low mobility into the amorphous regions of the polymer, and can therefore continue to undergo chemical reactions for many months and beyond. This time-dependent free-radical reaction mechanism poses serious concern for the radiation degradation of polymers, especially in the presence of oxygen as is observed in the reactions showed in Figure 10 (reactions 2 and 3), which has a high diffusional mobility and is very reactive with the radicals. Hydroperoxides also are formed as the first product of oxidation and upon their decomposition free radicals are re-generated (reaction 4 in Figure 10). Every molecule of hydroperoxide produced subsequently undergoes radiolysis to generate an alkoxy radical which both provides new initiating radicals and at the same time produces carbonyl compounds (reaction 5 in Figure 10). Thus, the process is autocatalytic and can lead to the further formation ketones, alcohols, esters, and carboxylic acids in the polyethylene chains. Therefore, as long as there is an oxygen source, the cycle can continue and the number of oxidation products will increase without any further irradiation (Schanbel, 1981). This process is known as post-irradiation aging and has been shown to occur in implants that were gamma sterilized in air and packaged in air-permeable packaging. Changes in physical, chemical and mechanical properties of UHMWPE as a consequence of oxidative degradation (Costa & P. Bracco, 2004). Property changes include an increase in percent crystallinity, an increase in density (an indirect measure of oxidation), an increase in elastic modulus, and a decrease in elongation to failure.

As the evidence of the clinical consequences of oxidative degradation of UHMWPE total joint replacement components increased, the orthopaedic implant manufacturers began to
study and then to employ alternative sterilization methods such as gamma radiation sterilization in inert environment (e.g. argon, nitrogen, vacuum) packaging as a means to minimize oxidation during shelf aging. For UHMWPE, cross-linking dominates when the polymer is irradiated in nitrogen, while chain scission dominates when the material is irradiated in air. This is due to the fact that oxygen is extremely reactive with the free radicals produced by irradiation, forming peroxides which can break down and lead to further radical production, so that the total number of free radicals generated and the total extent of chain scission, are greatly increased. It should be noted that, without some additional manufacturing step to extinguish any remaining entrapped free radicals, oxidation will occur upon exposure to oxygen (such as during in vivo use). For gamma sterilization in an inert environment to be successful, it must be combined with barrier packaging to prevent access of atmospheric oxygen to the UHMWPE during shelf storage. Thus, barrier packaging is expected to effectively reduce the risk of oxidative degradation of UHMWPE during shelf storage (Rimnac & Kurtz, 2005)

Fig. 10. Polyolefins oxidation caused by gamma sterilization

Polypropylene (PP) is one of the most widely used plastics for packaging applications. Polypropylene is one of the most popular polymers in the manufacturing of medical disposables, since it exhibits high transparency, good mechanical properties, low cost and chemical inertness over other polymers. In a continuously increasing part of this market, especially in the pharmaceutical area, but also in food packaging and especially in the manufacturing of syringes, security lenses, surgical clothing, etc. Medical instruments employed in the diagnosis or treatment of a patient, especially those that can penetrate the protective, barrier of the skin, must be completely exempt of germs.

Changes in polymer properties were observed when PP medical devices are sterilized by gamma irradiation undergoing oxidative degradation if sterilized in air. Oxidation of PP is usually relatively easy to detect owing to the strong absorption by the carbonyl group in the FT-IR spectrum as is showed in Figure 11. Polypropylene has a relatively simple spectrum
with few peaks at the carbonyl position. The integrated absorption of the C=O band centered about 1720 cm$^{-1}$ has been assumed to give a quantitative evaluation of the radiation induced oxidation. Since the PE is a polyolefin the carbonyl group is obtained in reaction 5 of the scheme in Figure 10. Oxidation tends to start at tertiary carbon atoms because the free radicals formed here are more stable and longer lasting, making them more susceptible to attack by oxygen. The carbonyl group can be further oxidized to break the chain, this weakens the material by lowering its molecular weight, and cracks start to grow in the regions affected.

Fig. 11. FT-IR spectrum of PP exposed to gamma sterilization in air

The changes in the PP molecule by gamma sterilization are associated with the changes in crystallinity and morphology of the polymer. The correlations between the changes in both morphology and crystallinity with other properties during irradiation are important to explain the mechanism that lead to crystallinity change. Some studies investigated the response of PP to $\gamma$-radiation and relate the crystallinity and morphological changes to corresponding changes in other properties such as mechanical properties, viscosity, melting temperature, etc. Kushal et al. (1995) relate the drop in the melting temperature, viscosity and mechanical properties versus the increases in crystallinity during $\gamma$-irradiation to the breakdown of crystallites with a concomitant formation of smaller crystalline entities.

The extent of chain scission and crosslinking of PP is dependent on the $\gamma$-irradiation dose but not the initial starting morphology (Zhang and Cameron 1999). Using WAXD (Wide angle X-ray diffraction) and DSC (Differential scanning calorimetry) techniques, Alariqi et al. (2006) found change in the degree of crystallinity, which caused by $\gamma$-irradiation, depends on the $\gamma$-irradiation dose (see Table 6) and Kostoski and Stojanovic (1995) found the increase in crystallinity of oriented isotactic polypropylene with low absorbed doses of $\gamma$-radiation, up to 200 kGy. They have also found that the peak melting temperature decreased with absorbed dose. The results were explained in terms of the scission of the tie molecules followed by the growth of new thin crystal lamellae, as well as to the fact that
irradiation produces defects in the polymer structure which decrease its thermal stability. However, the number of chain scission increased with decreasing the dose rate. From, lowering molecular weight, increased chain scissions, increased crystallinity, it can be understood that the rise in crystallinity is due to re-crystallization of shorter chains which are produced by the chain scission of tie molecules forming new perfect crystallites leading to an increase in crystallinity. On the other hand, the decrease in crystallinity was attributed to the formation of crosslinking. Krestev et al. (1986) have found that part of monoclinic α-phase of PP is converted into triclinic γ-phase during gamma irradiation. It was reported that the formation of γ-phase was not due to the crystallization of low molecular fraction but to the high internal pressure caused by the crosslinking.

<table>
<thead>
<tr>
<th>Irradiation dose (kGy)</th>
<th>Degree of crystallinity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WAXD</td>
</tr>
<tr>
<td>0</td>
<td>38.5</td>
</tr>
<tr>
<td>10</td>
<td>48.0</td>
</tr>
<tr>
<td>25</td>
<td>33.2</td>
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Table 6. Effect of gamma sterilization on crystallinity of Polypropylene

Polyisoprene, especially in the form of natural rubber latex, is widely used in prophylactic medical disposables, such as gloves and condoms, and found to be an effective barrier. Because of its unsaturation, natural rubber and many other elastomers will slightly crosslink when exposed to radiation sterilization conditions. Such crosslinking will not detract from the overall extensibility or elongation of these rubber devices. Natural rubber formulations, as well as formulations based on other elastomers, can also be used as gasketing materials in devices. Although isobutylene is well known to scission when exposed to radiation, a halogenated copolymer of isobutylene and isoprene, commonly brominated butyl rubber (BIIR), can be formulated to exhibit radiation response when used in the tyre industry. Having been previously crosslinked with a zinc oxide system, BIIR can withstand the radiation exposure required for sterilization. Such elastomeric materials form the sealed caps on injectable drugs, being able to reseal themselves after having been penetrated by the needle of a syringe.

Silicone rubber is widely used in medical applications, where sterilized is an essential requirement for all medical tools and devices that contact the body or bodily fluid and medical components must be sterilized frequently by gamma irradiation. Gamma radiation is known to induce changes in the molecular architecture of silicone rubber, resulting in an increase in molecular weight and a decrease in elasticity. This effect is also observed in samples previously subjected to post-cure treatments. Radicals are generated by chain scission and/or methyl or hydrogen abstraction (see Figure 12) and are subsequently terminated via oxidation reactions or coupled to form longer chain branches. Although these two mechanisms compete against each other, crosslinking reactions dominate in silicone materials; higher dosages of gamma radiation and longer treatment cycles have been shown to result in higher crosslink densities (Traeger & Castonguay, 1966). An increase in polymer-filler interfacial interactions through crosslinking reactions is also observed.
6.2 Action of stabilizers in polymeric medical device exposed to gamma sterilization

With the development of space science, the stability of polymeric materials against radiation has been drawing the attention of scientists. Polymers which contain aromatic groups are well known to have relatively good radiation stability, but are also very expensive. The practical solution of these protection tasks are connected to specific chemical agents, well engineered polymer additives, elaborated mainly for the stabilization of general purpose polymers. The radiation stabilizers, called “antirads” represent only a modest, but flourishing fraction of that thermo-oxidative- and UV stabilizers.

The reason behind the parallel technical development of conventional and radiation stabilizers is related to the fact, that the UV degradation and thermo-oxidative degradation as well as radiation degradation of polymers are all similar chain reactions. As such, these processes consist of several steps of: chain initiation, chain propagation, chain branching and chain termination. The scheme according to which these reactions proceed on a H containing polymer chain P is seen in Figure 6. In spite of the differences in fine details the task is similar in all the three main (thermooxidative, UV and radiation) degradation processes, namely to control and/or diminish the danger of deterioration of properties either by preventing chain initiation, and/or stopping chain propagation.

Additives may promote radiolytic stabilization on properties of polymers thought two primary mechanisms: a) scavenging of excited-state energy (quenching), and b) scavenging of paramagnetic species (free radicals, secondary electrons). Also the incorporation of additives, plasticizing type, act as "mobilizer" on polymer chains. Additives and stabilizers

Fig. 12. Effects of sterilization by gamma irradiation in silicone molecule
are commonly included in small amounts (less than 1%) in commercial polymer products to aid in processing, stabilize the material and impart particular properties to the product. In controlling the route of those oxidative chain reactions, there are two main types of antioxidant stabilizers:

- Primary or chain-breaking antioxidants interfere with the chain propagation step. That step is the main carrier of the oxidative degradation.
- Secondary or preventive antioxidants destroy hydro-peroxide groups, responsible for chain initiation and chain branching.

Typical primary antioxidants, interfering with the chain-carrying radicals are the orthodisubstituted phenols, alkylphenols, hydroxyphenyl propionates and hydroxybenzyl compounds. Irganox 1010 (see structure in Table 7) is one of the most important additive protecting PE and PP in radiation sterilization. It is important to note, that such stabilizers are never used alone. Secondary antioxidants represent an even greater group of sophisticated organic molecules: aromatic amines, organic sulfur compounds (typically thiobisphenols and thioethers) as well as phosmites and sterically hindered amines. These two latter type of compounds are successfully applied in the radiation-stabilization of PP (Williams et al., 1977). The Table 7 showed some commercial antioxidant structures.

Clearly, the radiation-protection stabilizer systems should fulfill a whole series of other requirements such as chemical, physical and toxicological safety. Take for example the blood-taking and transfusion sets, made out of plasticized PVC, radiation sterilized and then stored (standing by) for years, later filled with chemically stabilized blood, and cooled and stored again. During all these procedures the protected polymeric material should be stable, should not lose its elasticity, and in the last steps there are strict limitations on traces of all chemicals extractable by the blood.

In relation to radiation stability improvement, discoloration of PP homopolymer was eliminated by the incorporation of the light protector in the samples prepared by injection moulding. Samples of PP homopolymer with different additives also were prepared by compression moulding were irradiated to 25 kGy. The commercial additives used were Tinuvin 622, Irganox B225 (blend of Irganox 1010 and Irganox 168), Irganox PS800 and Irganox 1010. The structures of these commercial additives were showed in Table 7. Elongation to break was measured after irradiation and at 12 months of aging at room temperature. Previous experiments with samples prepared in the same way without additives had shown a strong effect of post irradiation degradation and this effect could be anticipated by the effect of a higher applied dose. The effect of additives was significant as all of additived samples could be considered functional after aging. Addition of antioxidants improved mechanical stability in samples prepared by compression molding and by injection moulding, but they had a negative effect in discoloration (Gonzales & Docters, 1999)

Hindered Amine Light Stabilizer (HALS) is among the more extensively used additives for protecting polymers against degradation by the combined effect of light, temperature, and atmospheric oxygen. The protection of the polymer from the light by these compounds takes place via a mechanism involving photo-oxidation of the amines to nitroxyl radicals (Lucarini et al, 1996). Nitroxy radical is capable of scavenging the radicals through a reaction called Denison cycle. On the other hand, very little information on this additive for
Table 7. Some commercial additives used in the stabilization of polymer gamma sterilized radiolytic stabilization of polymers has been published. The efficiency of a certain additive in the stabilization of polymer molecules against radiation may be evaluated by measuring the effect of this additive on the free radical population after irradiation, as well as on its rate of decay. The efficiency of HALS additives depends on their molecular weight, structure, solubility and concentration in the polymer matrix. Conversion of amines into nitroxy radicals following the reaction with peroxyl radicals leads to relatively stable intermediate species. Regeneration of the nitroxy radical limits the consumption of HALS.
during degradation allowing the use of these additives in low concentration. Tinuvin 622 (see structure in Table 7) is a macromolecular HALS, which exhibits a quite high thermal stability. This additive starts to decompose around 400°C with intramolecular ester group rearrangement. Final decomposition events occur at 900°C and include nitrile and hydrogen cyanide formation (Lucarini et al., 1996).

Samples of PMMA irradiated at 30 kGy and containing Tinuvin 622 showed more resistance to radiation damage. Tinuvin 622 also induces a faster evolution of radicals produced on PMMA radiolysis, which can result in the inhibition of free radical damage. Above 30 kGy, both PMMA without (PMMA-control) PMMA with Tinuvin 622 (PMMA-622) undergo significant changes in the yellowness index with increase of absorbed dose due to conjugated center that absorbs light in the visible range. After 63 days of storage at 30 kGy dose, the yellowness index measured was 2.78 and 0.17 to PMMA-control and PMMA-622, respectively. These results showed that the Tinuvin 622 is a good alternative for stabilizing the PMMA against gamma irradiation damage in sterilization processes with low cost (Aquino et al., 2010).

The scheme in Figure 13 is generally accepted to explain the aspects of the chemistry mechanism of HALS action to inhibit polymer photo-oxidation. This scheme was used to guide a strategy to assess Tinuvin 622 action in radiolytic stabilization of PMMA (Aquino & Araujo, 2008). According to this scheme, the tetramethylpiperidine moiety, which is the basic structure of HALS, is initially oxidized to produce a nitroxyl radical by gamma irradiation. The nitroxyl radical acts as a scavenger of the radical originating from the irradiation of polymer chain substrate to form an alkylated aminoether. From the aminoether, the nitroxyl radical is regenerated through quenching another peroxyradical produced by oxidation of the polymer chain. Thus the nitroxyl radicals could regenerate many times through the chain reaction before their depletion.

![Fig. 13. Typical photo-stabilizing action of HALS in the polymer system](image)

The single Electron Spin Resonance (ESR) spectrum was obtained for Tinuvin 622 sample irradiated at 100 kGy and was attributed to nitroxyl radical (Aquino et al., 2010). The chemistry of HALS had been widely documented for UV irradiation. As the Tinuvin 622 is a tertiary HALS a sequence of reactions starting with amine ionization and α-aminoalkyl radicals are formed. These radicals rapidly react with oxygen and fragment under the elimination of formaldehyde to nitroxyl radicals. Thus, similar stabilization mechanism is attributed to Tinuvin 622 when the PMMA is submitted to gamma irradiation. The gamma rays can break covalent bonds in PMMA molecule to directly produce the free radicals as was shown in Figure 8 (II). The gamma rays can also produce excited states in PMMA which undergo further reactions to produce the A radical (Figure 8) indirectly. Thus, there are two ways for Tinuvin 622 to decrease the main scission effect of gamma-irradiated PMMA. One
way is to directly inhibit the formation of A radical by quencher mechanism when Tinuvin 622 may be to absorb the energy of the excited molecules in PMMA via an intermolecular energy transfer and possibly convert the absorbed energy. The other way is based on ESR results, the A radical to be scavenged by a nitroxy radical and an alkylxoyamine is formed. The alkylxoyamine scavenges a peroxyl radical in a second step, in which the nitroxy radical is regenerated (Aquino & Araujo, 2008).

Vinhas et al. (2004) also reported radio-protective action of a common photo-oxidative stabilizer, HALS, in PVC films plasticized with DEHP (di-2-ethylhexyl phthalate). The HALS additive is believed to interrupt oxidative propagation reaction by scavenging of chlorine radical formed in PVC radiolysis.

On the other hand polymer blends are an attractive route to formation of a novel material. Polystyrene, PS, contains aromatic groups that increase radiation resistance and stabilizes the excited species formed by irradiation. The presence of PS in PVC/PS blends could be an interesting route to PVC radiolytic stabilization. The analysis of Figure 14 revealed that at 0-15 kGy the main effect of gamma irradiation on PVC is crosslinking and at 25-100 kGy the main chain effect is predominant. However, the PS in the blend system inhibits crosslinking in the lower irradiation dose range (0-15 kGy) and less chain scission occurs in PVC/PS film than in PVC film. At a sterilization dose (25 kGy) were found a decrease of 65% (95/05) and 47% (90/10) in scissions per original molecule of PVC (Silva et al, 2008). The PS molecule acts as an additive and the aromatic groups of PS structure absorb the excitation energy and a lower bond cleavage yield is noted. This in turn causes a decrease in the formation of free radicals, which are responsible for scission degradation reaction. The mechanisms of main scission and crosslinking of PVC have been showed in Figure 7.

Fig. 14. Reciprocal of $M_v$ as a function of the irradiation dose of PVC and PVC/PS blends
In addition, the preparation of polymer films containing disperse nanoparticles has a great interest. The importance of these nanocomposites is due to the mechanical, electrical, thermal, optical, electrochemical, catalytic properties that will differ markedly from that of the component materials. For example, the synthesis of Sb$_2$S$_3$ nanoparticles by sonochemical route under ambient air from solution containing antimony chloride as metal source and thioacetamide as a sulfur source produced amorphous powder with monodisperse nanospheres, whose diameters were calculated in the range of 300-500 nm. Films of PVC with Sb$_2$S$_3$ (PVC/Sb) nanoparticles were exposed to gamma irradiation at sterilization dose and the effects of the nanoparticles on the viscosity average molar mass (M$_v$) of sterilized PVC were studied. The results revealed less chain scissions occur in PVC/Sb films at 0.30 wt% concentration. At sterilization dose (25 kGy) was calculated a decrease of 67% in scissions per original molecule of PVC. No information about use of Sb$_2$S$_3$ in the radiolytic stabilization of polymers has been published and consequently the mechanism of radiolytic stabilization effect of these nanoparticles is not clear. However, some probable reactions may be going on under gamma irradiation.

7. Conclusion

Sterilization is defined as any process that effectively kills or eliminates almost all microorganisms like fungi, bacteria, viruses, spore forms. Gamma radiation sterilization are mainly used for the sterilization of pharmaceuticals. Depending on their different mechanism of actions, this sterilization method affects the pharmaceutical formulations in different ways. Thus, the sterilization method chosen must be compatible with the item to be sterilized to avoid damage.

Radiation processing has been used commercially for almost forty years. Gamma radiation from cobalt-60 is used to sterilize the medical devices used in operations and other healthcare treatments. Implants, artificial joints, syringes, blood-bags, gowns, bottle teats for premature baby units and dressings are all sterilized using radiation. Gamma irradiation is a physical means of decontamination, because it kills bacteria by breaking down bacterial DNA, inhibiting bacterial division.

The radiation resistance of a microorganism is measured by the so-called decimal reduction dose (D$_{10}$ value), which is defined as the radiation dose (kGy) required to kill 90% of the total number. Survival fraction of the microorganisms is reversely proportional with the absorbed dose. Doses for sterilization should be chosen according to the initial bioburden, sterility assurance level (SAL) and the radiosensitivity of microorganisms. Temperature plays a major role in the radiosensitivity of microorganisms. As a general rule, microorganisms are less radiosensitive when irradiated at low temperatures.

On the other hand, radiation sterilization of tissue grafts has been implemented in some tissue banks, and a dose of 25 kGy has been used in many of these tissue banks. The advantage of radiation sterilization is that it allows the processing of grafts, which have been previously sealed or tightly closed in special wrappings. Such procedures prevent any accidental recontamination during packing. Food also can is sterilized by gamma irradiation and the process exposing food to ionizing radiation to destroy microorganisms, bacteria, viruses, or insects that might be present in the food. Irradiated food does not become radioactive, but in some cases there may be subtle chemical changes. The use of low-level
irradiation as an alternative treatment to pesticides for fruits and vegetables that are considered hosts to a number of insect pests including fruit flies and seed weevils. The irradiation produces no greater nutrient loss than what occurs in other processing methods. However, the irradiation reduces the vitamin content of food, the effect of which may be indirect in that inadequate amounts of antioxidant vitamins (such as C, E, and β-carotene) may be available to counteract the effects of free radicals generated by normal cell metabolism. In addition, the most affected lipids during irradiation are thus the polyunsaturated fatty acids that bear two or more double bonds.

When radiation is used for the sterilization of medical devices, the compatibility of all of the components has to be considered. Ionizing radiation not only kills microorganisms but also affects material properties. When the polymer systems are submitted to sterilization by gamma radiation (25 kGy dose), their molecular structures undergo modification mainly as a result of main chain scission and crosslinking effects. Both processes coexist and either one may be predominant depending not only upon the chemical structure of the polymer, but also upon the conditions like temperature, environment, dose rate, etc., under which irradiation is performed.

The protection of polymers against sterilization dose requires efficient additives preventing and/or stopping chain reaction type oxidative degradation. Primary and secondary antioxidants work well here in synergy. Polymer blend and nanoparticles also may be used in radiolytic stabilization of polymer used in medical devices. Commercial raw materials are available for radiation-sterilizable medical devices made of polyolefins and other thermoplastics. Similarly, polymer compounds of suitable formulae are offered commercially for high-dose applications in nuclear installations.

8. References


Sterilization by Gamma Irradiation


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This book brings new research insights on the properties and behavior of gamma radiation, studies from a wide range of options of gamma radiation applications in Nuclear Physics, industrial processes, Environmental Science, Radiation Biology, Radiation Chemistry, Agriculture and Forestry, sterilization, food industry, as well as the review of both advantages and problems that are present in these applications. The book is primarily intended for scientific workers who have contacts with gamma radiation, such as staff working in nuclear power plants, manufacturing industries and civil engineers, medical equipment manufacturers, oncologists, radiation therapists, dental professionals, universities and the military, as well as those who intend to enter the world of applications and problems of gamma radiation. Because of the global importance of gamma radiation, the content of this book will be interesting for the wider audience as well.

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