

STERILIZATION, DISINFECTION, & ASEPSIS

Sterility and *asepsis* are different conditions. *Sterility* indicates the elimination of all viable life forms and their germinative elements such as eggs and spores. Sterility is absolute; there is no such thing as an object being “partially sterile”, whereas *asepsis* generally means that only certain types of life forms have been removed, excluded or neutralized (rendered non-viable), while the presence of other organisms may be tolerated or even promoted. For this reason, sterility is generally much easier to achieve and maintain than asepsis. The common process of *pasteurization* of food does not kill all microorganisms in the food. The objective of pasteurization is to achieve a “log reduction” in the total number of viable organisms. Subsequent refrigeration or freezing is intended to maintain the microorganism population at low numbers for long enough to allow consumption without causing disease, but over time the numbers of microorganisms and their metabolic byproducts, some of which are toxic, will inexorably increase. *Disinfection* refers to a process whereby many or all pathogenic microorganisms are neutralized or removed. The American Society for Microbiology (ASM) and the Centers for Disease Control (CDC) have posted guidelines that state “...the term “partially sterile” should not appear in the technical and commercial literature”. Unlike sterilization, disinfection can be achieved at varying levels as defined by the Centers for Disease Control:

High-level disinfectants are chemical sterilants which may be used for a shorter exposure period than would be required for sterilization to kill all microorganisms with the exception of high numbers of bacterial spores. Examples of the most resistant organisms dealt with effectively at this level include *geobacillus stearothermophilus* and *bacillus atrophaeus*.

Intermediate-level disinfectants will kill mycobacteria, vegetative bacteria, most viruses, and most fungi but do not kill all bacterial spores. Examples of the most resistant organisms dealt with effectively at this level include mycobacterium tuberculosis, polio virus, coxsackle virus, rhinovirus, *aspergillus*, and *candida*.

Low-level disinfectants kill most vegetative bacteria, some fungi, and some viruses. Examples of the most resistant organisms dealt with effectively at this level include *staphylococcus* species, *pseudomonas* species, *salmonella* species, human immunodeficiency virus (HIV), herpes simplex virus, hepatitis B, hepatitis C, and coronavirus.

The various levels of disinfection are possible because different classes of microorganisms tend to have different levels of resistance to germicidal agents. The most resistant are bacterial spores, followed by mycobacteria, then non-lipid or small viruses, then fungi, then vegetative bacteria, and finally the most susceptible to most germicidal agents are the lipid or medium-sized viruses.

The Rational Approach to Disinfection and Sterilization

In 1968 Earle Spaulding proposed a rational approach to disinfection and sterilization of patient-care items and medical equipment that has been widely adopted by infection control professionals because it is clear and logical. Spaulding proposed that the level of disinfection for each object should be based upon the intended use. This has evolved to three categories known as Spaulding's Classification: critical, semicritical, and noncritical.

Critical items are those that enter sterile tissues, cavities, or the vascular system or through which blood flows, such as blood delivery and filtration devices, implanted medical devices, and hypodermic needles; these must be sterile when used.

Semicritical items are those that touch mucous membranes or non-intact skin, such as endoscopes or wound dressings; for these items sterilization is preferred, but where that is not possible then high-level disinfection is required.

Noncritical items are those that only contact intact skin, such as bedpans, blood pressure cuffs, and hospital furniture; these require only low-level disinfection.

Sterilization and Disinfection vs. Asepsis

Like the difference between sterility and various levels of disinfection, the need for sterility vs. asepsis depends upon the application. For example, the objective for most clinical and surgical instruments and food handling equipment is sterility or disinfection, whereas many foods require live cultures of specific microorganisms at some stage of their processing or storage. In most cases it is necessary to take specific measures to ensure that only the desired microorganisms are present while excluding the undesirable ones. Complicating this is the fact that the desired organisms are often more fragile than the ones that are to be excluded. Many higher organisms, from termites to humans, have symbiotic relationships with microorganisms that are in some cases obligatory, being essential to the survival of one or both of the organisms concerned. The host organisms can become *septic* when invaded by damaging organisms, or when an unusually great number of otherwise helpful microorganisms are present.

The microorganisms and other biological agents of interest may include eukaryotic cells, bacteria, trypanosomes, protozoa, yeasts, molds & fungi, prions, viruses, and microscopic parasites such as mites and worms, as well as the eggs, spores, or other viable replicative agents from any of these. The processes used to achieve both sterility and asepsis are often quite different from those used to achieve disinfection, cleanliness, purity, or the reduction of toxins. Achieving sterility is fairly straightforward (for example: kill everything in a defined volume and exclude all further contamination or create conditions incompatible with life), whereas

achieving and maintaining asepsis is somewhat more complex (for example: selectively neutralize certain classes of microorganisms, but allow others to flourish, at least in some defined areas of the volume in question, while simultaneously allowing the necessary bidirectional flux of energy and matter to maintain this condition). Thus, both sterility and asepsis can be viewed as generalizations of circumstances under which the state of viable life forms is controlled in a specified volume. This is a consideration in a wide range of areas such as: cookware, food processing & storage, agricultural products, medical products, cosmetics, many consumer products (even play sand is often treated to assure sterility), scientific samples, cell and tissue culture, and some sensitive electronic devices.

Over the years a variety of methods have been employed to achieve sterility, disinfection, and asepsis, many of which are still in use today. No single process is suitable for every application, so it is important to understand each of the available processes and the circumstances under which the process may be advantageous or inappropriate. Also, the interaction between the process and the materials must be considered. For example, it is usually considered desirable that sterilization processes do not alter the properties of the material being sterilized. However, in

METHODS OF STERILIZATION

The methods of sterilization in common use can be grouped as follows:

Ionizing Radiation

- Gamma ray sterilization
- Electron Beam (E-Beam) Sterilization
- X-ray sterilization
- Ultra Violet Light

High-Energy Pulsed Light

Gas and Gas/Plasma Sterilization

- Ethylene Oxide (EtO or EO gas sterilization)
- LTHPGP (low-temp hydrogen peroxide gas plasma)
- Plasma (gas plasma) Sterilization
- Chlorine dioxide gas sterilization
- Ozonation and strong oxidizers

Mechanical, temperature, moisture, and pressure

- Autoclave, steam, moist heat and pressure sterilization
- Boiling, Dry heat
- Microwave Sterilization
- Direct heat, flame
- Cold sterilization
- Dessication

some cases the sterilizing process can have beneficial effects on the material being sterilized, beyond the sterilizing effect itself. One example of this is that some plastics will gain improved mechanical characteristics as the result of exposure to ionizing radiation. Other examples include the removal of non-biological toxic contaminants from a material during disinfection, such as when soaking an object in an ethanol-water solution for disinfection also has the desirable effect of removing petroleum-based oils from a cell-contacting surface. An example of an undesirable process-material interaction would include materials which tend to neutralize or absorb the sterilizing agent, such as cellulose when exposed to hydrogen peroxide during gas sterilization. These effects can be complex, and it is essential to test each material with each process, and to control the duration, dose, dose rate, and other parameters of the sterilization process to verify that the desired result is obtained. The following information is intended as a set of general guidelines. For critical applications the anticipated results need to be experimentally verified. More detailed information is available in the Resources section at the end of this chapter.

- Refrigeration, Freezing
- Freeze-drying, lyophilization
- Grinding & shaking
- Pressure
- Acoustic energy: sonic and ultrasonic

Disinfectants

- Alcohol/water solutions
- Ammonia; hot & cold, Quaternary ammonium compounds
- Chlorine (bleach) solutions (10% chlorine in water)
- Chlorine releasing compounds
- Hydrogen peroxide
- Iodine: gas, dry, moist solutions, Betadine
- Wetting agents, surface tension depression (Otto Rahn)
- Sodium carbonate crystals
- Glutaraldehyde, Vesphene

Bioactive agents

- Antibiotic, Antimycotic, Antiviral

Filtration, barrier, selective mechanical exclusion

- Microbial barriers, Particulate ionization and entrapment
- Liquid Media filters, Gas filters, Face masks: N95, SCBA,...
- BSI: gloves (latex, Nitrile, ...)

Competitive Biological Displacement

- Establishment of a dominant culture that resists septic invasion

Methods of Sterilization and Septic Control

The following sections give brief descriptions of the general classes of methods that are currently employed to achieve sterility, disinfection, or asepsis. One important aspect of these processes is the way they interact with the materials being processed. In some cases the process is inappropriate because either it causes an undesirable change in the properties of the material, or it can result in decomposition products that may damage or contaminate other materials, including biological or food materials that are sterilized while hermetically packaged. Changes in material properties can sometimes be tolerated, such as changes in surface color (staining), whereas in other cases the changes may result in device or system failure. In some cases, the sterilization process may actually result in measurable improvement in the properties of the material. One example of this is the cross-linking of some polymers by exposure to ionizing radiation, which may actually increase the material strength in a desirable way. Another example is the leaching of toxic chemicals from plastics during various disinfection or sterilization processes, thereby actually improving their biocompatibility for certain applications such as cell culture.

The most commonly used processes for achieving sterility, disinfection, or asepsis include gamma radiation, electron-beam, steam and pressure (autoclaving), ethylene oxide gas, filtration, and the use of chemical disinfectants. The process employed in each application will depend upon the desired outcome and the material(s) being processed. Many non-standard processes have also been included in the following set of descriptions because they have been employed in the past, or they are emerging or currently under development for future use, or they may have advantages under very unusual circumstances. It is not uncommon to combine sterilization processes, so some of the more exotic processes may be of value if used in combination with more standard processes for unusual or especially demanding applications.

Ionizing Radiation

Radiation is energy that "radiates" from a source and travels through space and matter. Common forms of radiation include sound, visible light, and heat. In the context of sterilization the term *radiation* usually refers to ionizing radiation because it can produce ions (charged particles) in matter. Ionizing radiation is produced when unstable atoms emit (radiate) their excess energy or mass. These emissions take one of two general forms: particulate (i.e., mass given off with kinetic energy and sometimes a charge) and electromagnetic (like light, which has no mass and no charge). Alpha and beta radiation are charged particulate radiation. Alpha particles are composed of two protons and two neutrons (identical to a Helium nucleus) and are generally considered "non-penetrating" because they usually do not penetrate skin or clothing, and only travel short distances (a few centimeters) in air. Beta particles are individual electrons emitted from the nucleus (not the orbital electrons) of neutron-rich isotopes, and are considered moderately penetrating because they can penetrate skin to the germinal layer and cause damage to the living cellular structures at that level. Beta radiation can also travel several meters through the atmosphere. The blue glow sometimes seen in the water around nuclear fuel cores in a

reactor is called Cerenkov radiation, and is caused by high-energy beta particles. Gamma radiation and X-rays are both forms of electromagnetic radiation. Similar to visible light or microwaves but of much higher energy, Gamma and X-ray radiation are considered penetrating radiation because they can penetrate deeply into living tissues and many other materials, and can travel many meters through the atmosphere.

All types of ionizing radiation are thought to act through the same basic mechanisms to achieve sterilization. The mechanisms are categorized as *direct* and *indirect*. Direct mechanisms are those where the ionizing radiation acts directly on cellular components, whereas indirect mechanisms are those where the ionizing radiation produces radiolytic products such as water radicals (H⁺ and OH⁻), which in turn act upon the structures of the microorganism. The structural targets include primarily chromosomal DNA which is apparently damaged by these mechanisms rendering the cells non-viable, as well as cell membrane structures which may immediately disable the microorganisms. Because of the very reasonable concerns regarding the safety of irradiated food products, the effects of these forms of sterilization on foods, and any possible carry-over effects on humans have been extensively studied, with no evidence to date to indicate that these methods pose a health risk. Irradiation has been found effective in the reduction of E. coli, Salmonella, and Campylobacter contamination. Irradiation does not cause foods to become radioactive, but it does degrade the quality of some foods. For example, some dairy products develop undesirable changes in flavor as a result of irradiation, and some fruits become noticeably softer, such as nectarines and peaches.



The use of radiation to preserve foods has a long history; it was first reported in France in the 1920's. In 1964 the USFDA approved the use of irradiation to extend the shelf life of white potatoes. NASA has irradiated foods for astronauts since the 1970's. More recently, the FDA approved irradiation for red meat in 1997. The Radura (shown at left, it is green when printed in color) is the international symbol indicating that the labeled food has been irradiated. In the United States, the Radura symbol must be accompanied by the words "treated with radiation" or "treated by irradiation" on all irradiated food items. In addition

to food preservation, irradiation has been used to control the ripening and sprouting of intact grains, fruits and vegetables, and to inhibit insect damage.

Ionizing Radiation for sterilization of medical products and pasteurization of food on an industrial scale is usually in one of the following forms: (1) gamma radiation, (2) beta radiation, (3) electron beam or simply e-beam, and (4) X-ray. These forms of energy allow "cold" sterilization because heat is not directly applied to the material being sterilized. Due to the ambient temperatures and the penetrating nature of ionizing radiation, it is often possible to sterilize food, drugs, medical materials, equipment, and supplies after they have been packaged and hermetically sealed, thereby minimizing the chances of recontamination before use. In these applications it is important to consider the effects of the ionizing radiation on both the material being sterilized and the packaging material as well. Each cycle of radiation exposure is equivalent to an "aging treatment" of a polymer, wherein changes in color, stiffness, brittleness and other

properties may be observed. This results in part from polymer chain scission and cross-linking during irradiation. As a general rule, polymers that have an aromatic ring structure are more resistant to ionizing radiation than polymers with a predominantly aliphatic structure. Thus, polystyrene and polyimide both tend to resist ionizing radiation well, whereas polymers with carbon-carbon chains and hydrogen atoms attached will tend to cross-link, and tetra-substituted carbons along the polymer will tend to lead to chain scission.

Radiation dose for sterilization is expressed in units of megarads (Mrad) or kilograys (kGy). The units are energy per unit mass.

$$1 \text{ rad} = 0.01 \text{ Joule/kg} = 0.01 \text{ gray} = 100 \text{ ergs/gram}$$

$$1 \text{ gray} = 1 \text{ Joule of energy absorbed per kilogram of matter}$$

For sterilization processes it is common to categorize the dosage level as low (< 1 kGy), medium (1 – 10 kGy), or high (> 10 kGy).

GAMMA RADIATION

Gamma radiation has become the industry standard for radiation sterilization. Once a facility is set up to provide gamma irradiation, the cost of operation is relatively low and the sterilization results are excellent and reliable. It is a form of ionizing radiation, and as such, its mechanism of germicidal action is described above in the section titled “Ionizing Radiation”. Gamma Radiation for sterilization processes is usually provided by a radionuclide source such as Cobalt-60 (Co-60), with a dosage of typically 25 kGy (2.5 Mrad), often carried out at or only slightly above room temperature.

ELECTRON BEAM and BETA RADIATION

Beta particles are electrons that are emitted from atomic nuclei (not orbital electrons), whereas electron beams can be formed by stripping orbital electrons and projecting them as a beam using high-voltage plates and targets without the need for a radioactive source. Electrons from either source do not penetrate matter as deeply as gamma radiation, therefore it may be necessary to irradiate from several sides of larger objects to assure complete sterility. Manufacturers of e-beam sterilization equipment claim that e-beam causes less damage to polymeric materials than gamma radiation. The process of e-beam sterilization is generally faster than gamma sterilization (minutes vs. hours), but overall less is known about the effects of e-beams on materials and this process is less widely used than gamma irradiation for sterilization.

X-RAYS

X-rays are another form of ionizing radiation. Direct comparisons between the effectiveness of electron beam, gamma rays and X-rays in sterilization is difficult and often inconclusive because of differences in the doses applied and penetration depths. Electrons have a limited penetration depth of about 5 cm in food and soft tissues, while X-rays have significantly higher penetration depths (up to ~ 4 meters).

The use of X-rays to achieve microbial inactivation in foods has been studied extensively in Russia. Linear induction electron accelerators (LIEA) are fairly simple devices which produce X-rays by directing an electron beam toward a heavy metal target. The radiation source is electrically controlled, unlike radio nuclide sources such as Co-60 and Cs-137. This simplifies the facilities required for X-ray sterilization since heavy concrete shields and other continuously active safety features are not as essential. X-ray radiation has several other advantages: it can be directionally controlled, the radiation field can be shaped, and it is highly reproducible.

X-ray pulses can be delivered with a dose rate many orders of magnitude higher than is possible with Co-60 sources, and because X-rays are electrically controlled it is possible to effectively inactivate microorganisms with ultra-short, high-intensity X-ray radiation pulses. This results in transiently higher local radical concentrations which favors radical-radical recombination reactions, leading to less diffusion of radical species. This may reduce the negative effects on food that is processed using X-ray radiation rather than other forms of ionizing radiation, because the production of radical species are thought to be one of the responsible mechanisms for undesirable effects of irradiation on food quality.

The mechanism of germicidal action of X-rays is probably similar to that of radiation from radionuclides such as Co-60 or CS-137, because the X-ray energy spectrum from X-ray sources used for germicidal applications is broader than and generally overlaps with the discrete energy levels emitted from radionuclide sources.

ULTRAVIOLET LIGHT

Ultraviolet (UV) light has a wide range of applications in industrial processing, generally utilizing light in the wavelength range from 100 to 400 nm. Various subdivisions of this range are associated with different widely known effects. The UVA range (315 to 400 nm) is most commonly associated with effects in human skin that cause tanning. The UVB range (280 to 315 nm) has been implicated as a causative agent in sun burns and skin cancer. The UVC range (200 to 280 nm) is also known as the “germicidal range” since it effectively neutralizes or inactivates viruses and bacteria. The vacuum UV range (100 to 200 nm) is quickly absorbed by most substances including air, and thus can be transmitted long distances only in a vacuum.

For germicidal purposes, UV light is used in cell culture laboratories to treat the interior surfaces in biosafety cabinets, in the disinfection of water and food-contacting surfaces, and more recently in the processing of fruit juices (mainly apple juice and cider). UVC light has germicidal properties over the entire wavelength range of 200 nm - 280 nm, but UV fluorescent lamp bulbs that have been optimized for germicidal applications are commercially available with peak energy at 254 nm. The minimum effective exposure energy is ~ 400 J/m² throughout the cross section to be sterilized. Minimum exposure times vary from application to application. The mechanism of germicidal action is that lethal DNA mutations are caused by DNA absorption of the UV light, with subsequent cross-linking between neighboring pyrimidine nucleoside bases (cytosine and thymine) in individual DNA strands. This impairs formation of hydrogen bonds to the purine bases on the opposite DNA strands, thereby blocking transcription and eventually leading to cell death. The amount of cross-linking is proportional to the UV exposure. This mechanism of inactivation results in a sigmoidal curve of microbial population reduction. This “survival plot” relates the UV exposure (time and intensity) to the percentage of remaining viable microorganisms. Damage resulting from low

levels of UV exposure can be repaired by cellular mechanisms by some microorganisms, but cross-linking above a certain threshold results in cell death.

UV sterilization is often employed with other sterilization processes, such as the use of oxidizing agents (ozone or hydrogen peroxide), or chemical disinfectants. Because UV sterilization depends upon optical exposure to the incident light in the ultraviolet range, the optical properties of the object being sterilized must be considered carefully. Optical clarity in the visible range does not necessarily imply optical transmission in the UV range, and the incident light may be reflected or refracted, thus concentrating or reducing the total UV exposure in different locations. Internal cavities or the underside of objects exposed to UV light are most likely to retain viable microorganisms. The advantages of UV light as a sterilizing process include the ease of use, ease of shielding, low cost of installation, very low cost of use, minimal damage to substrate materials, and lack of surface residues.

UV exposure is described quantitatively by several terms. The *UV dose* or *fluence* is the total energy of all wavelengths of UV light passing from all directions through an infinitesimally small sphere. Fluence divided by the time of exposure (seconds) is the *fluence rate*, which has units of power. Thus fluence rate refers to the total UV power passing through a volume of space from any direction, as opposed to *irradiance*, which refers to the power passing through a surface. With no optical scattering or reflection, for a perfectly parallel beam that is perpendicularly incident on the surface, irradiance and fluence rate are identical. The appropriate quantity to consider for UV disinfection is the UV fluence rate because in practical applications a microorganism will receive UV power from multiple directions due to reflections, scattering and the use of multiple lamps.

HIGH-ENERGY PULSED LIGHT

High-energy pulsed light (HEPL) or broad-spectrum pulsed light (BSPL) is a technology generally applied to enhance the preservation of packaged foods, but can also be used for some pharmaceuticals and water. Short and intense pulses of broad spectrum white light, from near infrared (IR) into the ultraviolet (UV) region are employed. Most of the energy of the light is concentrated in the 170 to 2600 nm wavelength range. The light pulses are produced by such means as capacitive electrical discharge to high-intensity lamps, producing an energy density in the range of 0.01 to 50 J/cm² at the illuminated surface. Thus, the spectrum is similar to that of natural sunlight at sea level, but the intensity is as much as 20,000 times greater. Pulses of light are delivered at a rate of typically 1 to 20 pulses per second, each pulse lasting from 1 μs to 100 ms. The HEPL process can provide a high level of microbial inactivation on the surfaces of foods and packaging materials in just a fraction of a second, much more quickly than most other sterilization methods and with no undesirable residues as often results from the use of disinfectants. The depth of penetration into the food is generally low, so bulk sterilization of foods or other materials throughout their full thickness is generally not achieved unless the material is thin and transparent (such as water). HEPL can reduce or eliminate the need for the use of chemical disinfectants and preservatives for some processed foods, and can

improve the quality (by limiting chemical contamination) and/or extend the shelf-life of produce.

The efficacy of the HEPL process has been tested against many types of microorganisms, including bacteria (vegetative cells and spores), molds and fungi, viruses, and protozoa (PurePulse Technologies Inc. 1999). The process parameters are generally adjusted to the needs of each specific application. Certain wavelengths (such as UV) are known to be more effective than others in terms of lethality to the microorganisms, but UV light can also cause undesirable photochemical effects on the material to be sterilized. Longer wavelength light is more likely to cause photothermal (heating) effects, which may or may not be acceptable. Undesirable wavelengths can be filtered out as necessary. The antimicrobial mechanism of action of the pulsed light process is a function of both the high peak power and the broad-spectrum of the flash. Light in the UV spectrum targets DNA molecules, whereas other wavelengths have disabling effects on the microorganisms in different locations. The motility of many microorganisms is observed to halt abruptly after HEPL treatment, suggesting direct destructive effects on cell membranes, motor proteins, enzymes and other cellular structures in addition to the structural changes in DNA.

MICROWAVE RADIATION

The use of microwave radiation to sterilize food has been reported since about 1967. Microwaves range from ~300 MHz to 300 GHz in the electromagnetic spectrum. In principle, lower frequency radio waves could also be used although currently this process is rarely, if ever, used for sterilization or pasteurization of food. Microwave ovens used for domestic cooking operate at 2.45 GHz. In the United States, 915 MHz is also used for industrial microwave heating processes. Outside of the US, other microwave frequencies are also used for heating processes.

The mechanism of germicidal action is essentially heating by two mechanisms: dielectric and ionic. Dielectric heating is primarily due to the forced resonant oscillation of the dipolar structure of water. Ions will also be mechanically driven by the oscillating electromagnetic field, producing heat. Other possible non-thermal (athermal) mechanisms of microwave processing have been proposed. These include electroporation, cell membrane damage and rupture, and direct electromagnetic energy coupling leading to cell lysis. Scientific support for these mechanisms is not entirely convincing.

The rate of heat generation per unit volume of material can be characterized as:

$$Q = 2\pi f \epsilon_0 \epsilon_l E^2$$

where: f = frequency, ϵ_0 = the permittivity of free space (a universal constant), ϵ_l = the dielectric loss factor (a property of the material), and E = the strength of the electric field at the location of interest.

The main advantage of microwave heating for pasteurization and sterilization is simply that this form of heating happens much more quickly than conventional heating, especially for thick cross-section solid foods which, by conventional heating methods, would rely upon the slow process of conduction of heat from the exterior to the interior. The main problem with microwave heating processes is that they tend to yield non-uniform heating. To convince yourself of this, simply heat a pre-packaged frozen lasagna dinner according to the manufacturer's instructions, and dig in with caution. Certain areas will be extremely hot, while others will remain relatively cool. To achieve reliable sterilization, the heating would need to be nearly uniform throughout the

material. As it turns out, control of the uniformity of the microwave heating process is difficult to achieve, and as a result, microwave radiation facilities for food pasteurization and sterilization are large, complex, and costly.

OSCILLATING MAGNETIC FIELDS

Magnetic fields have been applied to microorganisms to study the effect on growth and other cellular processes. The magnetic fields are classified as either static or oscillating. Static magnetic fields are constant in time, whereas an oscillating magnetic field has a time-varying amplitude, usually sinusoidal. Many studies have been conducted and the results are highly variable, depending upon the organism being studied, the nature of the applied magnetic field, and many other factors. In some cases the fields induce more rapid growth, in others the growth rate is inhibited, and in many cases there is no detected effect at all. Oscillating magnetic fields have been specifically evaluated for their potential for inactivating microorganisms in packaged food and other materials. The magnetic field amplitudes are large, ranging from 5 to 50 Tesla. By comparison, the Earth's steady magnetic field ranges from 25 to 70 μ T. The fields are applied in pulses, with a frequency of 5 to 500 kHz. Though microorganism population reductions of up to 2-log cycles have been reported when subjected to magnetic fields of this nature, the results are difficult to replicate. The use of magnetic fields to reliably control microorganism populations is not currently a practical reality.

PULSED ELECTRIC FIELDS

Pulsed electric field processing (PEF), also known as high-intensity pulsed electric field, involves the application of pulses of high voltage electric fields, typically 2-8 kV/mm. The substance to be processed, such as food, is placed between 2 electrodes and exposed to the pulsed electric fields typically for less than one second, so this process is relatively fast compared with other sterilization processes. The waveform of the pulsed fields depends upon the equipment and application, and includes square waves, sine waves or exponentially decaying step functions, carried out at approximately room temperature. Total energy dissipation within foods processed by PEF is low, thus minimizing undesirable changes in appearance, taste, or nutritional quality. The use of PEF for food processing is (at the time of this writing) very limited, with less than 5 operational commercial facilities worldwide. There are several technical challenges and considerations when employing PEF. The treatment chambers and electrode systems must be designed to provide uniformly high fields to the substance being processed, to avoid damage in areas with concentrated fields, or conversely, process failure in areas with less field strength. The substance being processed must be considered carefully, as some materials are subject to rapid electrolytic degradation (electrolysis), and some materials will heat much more rapidly than others. The material to be processed must have low electrical conductivity, must not contain bubbles, and there are limits to the allowable particle size. The mechanism of germicidal action of PEF has been hypothesized to include electroporation of cell membranes leading to cell death, and "electrical breakdown" of key cellular components, but the exact mechanism of inactivation remains unclear. Quantitative evaluation of

PEF with food products demonstrates that it does not generally yield sterility, rather, there is a significant log reduction in the number of viable microorganisms. Thus, PEF would be considered as an alternative, for example, to Pasteurization and similar processes. The motivation for using PEF, in addition to the speed at which the process can be applied, is that proponents of the process assert that it results in less food degradation.

HIGH VOLTAGE ARC DISCHARGE

One of the earliest applications of electricity in germicidal processes for aqueous fluids is high-voltage arc discharge. The process is relatively simple: a rapid series of electric arcs are discharged in an electrode gap within the fluid. The resulting physical effects on the fluid, including electrolysis, are thought to inactivate the microorganisms in suspension between the electrodes and in the immediate vicinity. It is this widespread fluid degradation, however, that limits the usefulness of this process for food processing, because the widespread physical and chemical effects of the process, including the creation of highly-reactive chemical compounds, tend to irreversibly damage the food. At best, this process could yield a several log reduction in the numbers of microorganisms, so under some circumstances it may be considered as a potential alternative to Pasteurization or similar processes.

Heat, Steam & Pressure

STEAM STERILIZATION – AUTOCLAVE

Moist heat under pressure has been used extensively for sterilization. The specialized chamber for this application is commonly called an *autoclave*. Modern autoclaves range from small and simple desk-top systems to complex systems with large chambers for industrial scale processing. These systems often have controlled protocols, called *cycles*, which are selected by the user and then monitored to verify that the cycle was performed correctly. Different cycles can be selected for different types of materials, for example, surgical instruments vs. laboratory fluids vs. infectious biomedical waste tissues prior to disposal.

Autoclaving is considered acceptable for non-critical sterilization applications. The temperatures employed range from 115 °C and upward, so this process can easily damage thermoplastic materials.

DRY HEAT STERILIZATION

Dry heat is effective at inactivating microorganisms, but in general the temperatures required are higher than is required for steam sterilization to achieve an equivalent level of germicidal action. Dry-heat forced-air ovens used for sterilization are typically operated at 160 °C to 170 °C for 2 hours or longer to achieve adequate microbial inactivation. Many materials, including most commonly used plastics, can not withstand prolonged exposure to these temperatures, so dry heat is less frequently used when plastics or other heat labile materials are being sterilized. High temperatures may also have undesirable effects on some metals. These effects include accelerated aging of precipitation-hardening or solution heat-treated metals (most aluminum alloys, some stainless steel alloys such as 17-4 PH, etc.) which eventually would lead to loss of material properties, or surface effects such as accelerated oxidation. Also, dry heat is

inappropriate for sterilization of any material that must remain moist throughout the process, since dry heat will quickly evaporate aqueous fluids from most materials.

PASTEURIZATION

The common process of pasteurization of food, especially dairy products, is not intended to kill all microorganisms. The objective of pasteurization is only to achieve a "log reduction" in the total number of viable organisms. Subsequent refrigeration or freezing is intended to maintain the microorganism population at low numbers for long enough to allow consumption without causing disease, but over time the numbers of microorganisms and their metabolic byproducts, some of which are toxic, will inexorably increase. The commercial process of pasteurization of dairy products in the U.S. is regulated by the United States Department of Agriculture, therefore the terminology on the product label has a very specific meaning. For milk, if the product is labeled "pasteurized" that means that it was heated to 161.5 °F for at least 15 seconds. This is the most commonly used process and is called "high temperature-short time pasteurization" (HTST). Some products are labeled "ultra pasteurized" or "ultra-high temperature pasteurized" (UHT). In this process for milk it means the temperature reached at least 280 °F for at least two seconds. The higher temperature kills more microorganisms and thus increases the shelf life of the milk significantly: HTST pasteurized milk should be sold within 14-21 days after processing, whereas UHT milk has a shelf life of 45-55 days in standard packaging and up to six months in sealed aseptic boxes. Note that once the package is opened milk should be consumed within about a week, regardless of the type of pasteurization. The advantage of UHT pasteurization is that it facilitates cross-country shipment of dairy products simply because of the increased shelf life. Opponents of UHT pasteurization, mainly consumers of "organic" foods, point out that the UHT process is potentially damaging to the quality of the milk, and promotes national food distribution practices rather than local/regional food production and consumption.

ULTRASOUND

Ultrasound is mechanical energy generated by sound waves at a frequency of 20 kHz or higher. Ultrasonic energy is widely used industrially for range detection, imaging, thickness measurement, crack detection, weld inspection, cleaning and welding, especially of thermoplastics, and under some circumstances can also be used to inactivate some enzymes and microorganisms. The germicidal mechanism of action of ultrasound is thought to be intracellular cavitation which results in micromechanical damage to cellular structures when the microscopic cavitation bubbles collapse, leading to cell lysis. Cavitation is a powerful mechanical process, causing significant damage to metal and ceramic components in water flow systems, including piping, propellers, and even sluices, so it is certainly reasonable to expect that intracellular cavitation, if it does occur, would be extremely damaging to most cellular structures. On the other hand, medical ultrasonic imaging is known to be non-damaging to tissues and body fluids, so under a wide range of exposures ultrasonic energy would not be expected to be harmful to most microorganisms. There is very little

quantitative data on the intracellular effects of ultrasound when employed as a means to inactivate microorganisms. When used in the food industry, ultrasonic energy would need to be combined with other preservation processes such as heat and pressure, in part because it would be difficult or impossible to guarantee uniform exposure of the substance to the ultrasonic energy throughout its volume. With non-homogeneous materials such as most foods, the presence of particles and other interfering structures can shield some spaces within the material from much of the ultrasonic energy. This is called an ultrasound shadow region. At this time, ultrasonic energy for use in food preservation is under development and is not widely in use on an industrial scale.

OHMIC AND INDUCTIVE HEATING

Ohmic heating is known by many names, including Joule heating, electrical resistance heating, direct electrical resistance heating, electroheating and electroconductive heating. In this process electric currents are passed through a substance with some electrical resistivity, with the objective of heating the substance directly by resistive heat loss. The thermal power (W) generated by this process depends both upon the total resistance (R) of the substance and the total electrical current (I) applied, by the relationship:

$$W = I^2R$$

The rate at which the substance will be heated depends among other things upon the total mass and the specific heat of the material, minus any thermal loss that occurs during the heating process.

Ohmic heating is different from inductive heating. In Ohmic heating, electrodes directly contact the substance being processed and electrical current is passed directly through the substance. Inductive heating is less direct: electrical currents are induced by rapidly oscillating electromagnetic fields such as radio frequency energy, so it is not necessary for electrodes to contact the substance directly. This has the potential benefit of allowing foods to be heated by induction after packaging to enhance preservation. However, data on the effectiveness of inductive heating of foods for germicidal action are scarce. There are many potential applications of Ohmic heating, including blanching, evaporation, dehydration, fermentation and extraction. The primary advantage usually claimed for Ohmic heating is its ability to heat materials rapidly and uniformly, even impure and non-homogeneous substances. The mechanism of germicidal inactivation in Ohmic heating is thermal, though there are some claims of other non-thermal effects such as electroporation.

HIGH PRESSURE PROCESSING

High pressure processing (HPP), is also known as high hydrostatic pressure (HHP) or ultra high pressure (UHP) processing. In this process, foods are subjected to pressures between 100 MPa and 800 MPa. The foods can be either liquid or solid, and may even be already packaged. The process can be carried out at low temperatures (below 0°C) through room temperature, up to and beyond 100°C. The process of compression generally tends to increase the temperature of foods by *adiabatic heating* by ~ 3°C/100 MPa. Other effects of the HPP process include changes in the pH of foods and possible other chemical changes which generally increase with increasing process temperature and treatment duration. The substances are exposed to the high pressure either as a brief pulse (as short as 1 ms) to over 20 minutes in duration. One significant

advantage of HPP is that it acts uniformly throughout the substance regardless of total mass, shape, or presence of inhomogeneities.

Water activity (the relative availability of water in a substance), pressure, duration, temperature, compression and decompression rate and pH are critical process factors in determining the germicidal action of HPP. Food pathogens and spoilage microbes are inactivated when temperatures of 45 °C or greater are employed. Higher temperatures (~100 °C) and pressures (700 MPa) are used to inactivate spore forming bacteria such as *Clostridium botulinum*. But it is important to note that some bacterial spores are resistant to the extreme parameter ranges employed in HPP, so the process does not guarantee sterility under any conditions.

Gas and Gas/Plasma Sterilization

ETHYLENE OXIDE (EtO or EO Sterilization)

Ethylene oxide gas sterilization is widely used because it is less damaging to sensitive materials such as electronics and many plastics that would be damaged or destroyed by exposure to ionizing radiation or steam sterilization. This is because it can be performed at low temperatures (generally less than 60 °C), and the absorbed sterilant gasses tend to be non-damaging and usually evaporate quickly when the sterilized materials are removed from the sterilization chamber. For a wide range of materials, EO gas has no measurable negative effects on appearance or material properties.

Some materials have high gas permeability and low absorption of EO gas and therefore can be used almost immediately following sterilization (example Tyvek sheet), whereas some materials have a tendency to retain ethylene oxide residue for some period of time after sterilization, for example, PVC. In the latter case, or advisedly if the absorption and release rate of EO residue is unknown, it is common practice to quarantine the freshly-sterilized objects, typically for 7-14 days, to allow complete removal of EO gas residue.

The mechanism of germicidal action of EO gas is a chemical reaction in which the gas causes alkylation and subsequent denaturing of nucleic acids and proteins, including enzymes critical for life. This reaction is temperature dependant, and generally to be effective the correct amount of water/EO gas concentration must be maintained. The process can be time consuming, often requiring a pre-conditioning cycle of 24 hours at controlled temperature and relative humidity, followed by atmospheric evacuation and introduction of EO gas for several hours, followed by flushing with air or nitrogen to remove any remaining EO gas.

EO gas is considered a carcinogen and mutagen, and should be handled with caution. Many facilities require constant monitoring of air quality when EO gas is in use, with sensitive gas monitors operating continuously in rooms where EO gas exposure is a potential occupational hazard. EO gas is also highly flammable. For this reason it is frequently diluted with either carbon dioxide or fluorocarbons.

LTHPGP

Low-temperature hydrogen peroxide gas plasma sterilization (LTHPGP) is a low-temperature method of oxidative sterilization for medical devices and surgical instruments that is considered to be safer than EtO gas because the only byproducts are water vapor and oxygen, with no toxic residues. The other advantage of this method over EtO gas is that the sterilization times are significantly shorter, ranging from 1-4 hours as opposed to ~24 hours for EtO gas. The method of hydrogen peroxide plasma sterilization was developed by Advanced Sterilization Products (ASP) in the early 1980s and is marketed under the trade name STERRAD™. Hydrogen peroxide plasma sterilization uses a small volume of 58% hydrogen peroxide which is vaporized in the sterilization chamber and converted to a low-temperature plasma phase through the use of radio frequency (RF) energy. The charged plasma particles, ultraviolet light and free radicals that result effectively sterilize instruments in about one hour without producing toxic residues or emissions. Hydrogen peroxide plasma sterilization is generally used in smaller volume areas, such as in hospital and laboratory sterilization, because it is not as effective in large-volume industrial-scale applications. LTHPGP technology is well suited to heat-sensitive materials and moisture-sensitive instruments. The process includes five phases: (1) the vacuum phase, (2) the injection phase in which a small amount of liquid hydrogen peroxide is injected into the chamber, which quickly evaporates, disperses and rapidly kills bacteria on readily exposed surfaces, (3) the diffusion phase in which the hydrogen peroxide vapor permeates the chamber, exposing all surfaces to the gas-phase hydrogen peroxide sterilant, providing more thorough sterilization without leaving any toxic residues, (4) the plasma phase, during which the chamber pressure is further reduced and the remaining hydrogen peroxide vapor is converted to a low-temperature plasma cloud that contains ultraviolet light and free radicals. After the ionizing energy is cut off the activated components gradually lose their high energy and recombine to form oxygen and water. At this point, phases 1, 2, and 3 are repeated for optimal sterilization. The final phase, (5) the vent phase, is simply where the chamber pressure is returned to ambient pressure, and the sterilized objects are immediately ready for use with no need for cool-down, degassing or aeration.

Disinfectants

Chemical disinfectants are widely used in industry, medical and clinical settings, laboratory settings, and in the household.

Chemical disinfectants can have damaging effects on a wide range of materials, including many plastics, composites, and metals, even stainless steel. The industry standard test for the effects of chemical agents on a material is the Environmental Stress Crack Resistance (ESCR) test. In this test a sample specimen of specified dimensions is mechanically scratched or scored, then subjected to a range of mechanical strains, then immersed in the chemical agent being tested. The specimens can then be evaluated for failure, typically by a quantitative measure such as elongation-at-failure. The ESCR test is widely employed, but it is important to note that the in-service results are dependant upon many factors related to the overall service environment of the material, which includes the duration of exposure to the chemical agent the stress history, temperature

cycling, and many other factors which may exacerbate the effect of the chemical agent on the material being tested.

Filtration, barrier, & selective particulate exclusion

FLUID FILTERS

All of the previously discussed methods and processes for microbial control were essentially based upon the inactivation of undesirable microorganisms. For these processes it is incorrect to state that the microorganisms have been removed, since they are still present but are no longer viable. For many industrial and biomedical processes microbial inactivation is sufficient, but for some applications it is important to remove or exclude the organisms altogether. These applications include the manufacture of precision optics and micro-electronics, because each microorganism acts as a particulate contaminant. It is in this capacity as a contaminant particle, and not so much as an etiological agent, that high purity industrial process must also exclude microorganisms. Many industrial processes also use yeast and bacteria actively as agents in the process. For some of these processes the presence of the microorganism in the final product is undesirable, so at some point they must be removed. One example is in the brewing industry, where the yeast cells and other solid byproducts of fermentation are removed by filtration before final packaging. The American brewing industry was instrumental in the development of low-cost sub-micron pore sized filtration technology for use on an industrial scale. The biomedical industry and basic researchers alike use filters with standard guaranteed maximum pore sizes of 0.22 μm and 0.10 μm , small enough to exclude all bacteria, spores, yeast and fungi while allowing liquids and gasses to pass relatively freely. By this means it is possible to achieve sterility by the total exclusion of microorganisms larger than a specified size. Filters commercially are available to accommodate large industrial processing equipment as well as standard cell culture plastic containers, Luer fittings (the tapered press fittings on syringes and IV tubing), and other small-scale applications. Many of these filters are inexpensive enough to allow one-time use and are disposable. It is important to note that filters will indiscriminately remove particles too large to pass through the pore size, so certain particulate-bearing fluids, such as whole blood and aqueous cell suspensions, can not be filter sterilized because the essential cellular components such as red blood cells and platelets would also be excluded, whereas it is common practice to filter-sterilize other biofluids such as blood serum, saline solutions, cell culture media, and gasses, when the only desired constituents are all in solution with no intended particulate content.

Filter manufacturers state that even large proteins can freely pass through sub-micron filters, so the protein content of biofluids should not be altered by filtration. Of course this also means that certain types of biological agents could also pass through the same pores, for example prions, which are themselves just a protein molecule, as well as the non-particulate toxins that may have accompanied or been produced by the microorganisms. Sub-micron filters can become rapidly clogged if protein-rich solutions are allowed to air dry on the filter membrane between filtration cycles, even though these same proteins would readily pass the filter if they were in solution.

Interaction of Materials and Sterilization Processes

A table showing the effects of various sterilization and disinfection processes on different materials is provided below. Though this material-process interaction has been widely researched, comprehensive published data are difficult to obtain. The table is therefore incomplete, and further, it is intended as an initial guideline. It is very important to carefully select not just the appropriate material, but also specific grades of the desired material which have been developed to provide enhanced resistance to common sterilization processes. Testing of each selected material with each intended process is highly advisable, regardless of manufacturer claims.

The table contains a large number of materials, some of which are more commonly used in biomedical applications where sterilization and disinfection processes are more critical. According to Medical Device Technology, September 1995, the top ten plastics used in medical devices are:

- 1- Polypropylene
- 2- Polyethylene
- 3- Silicone elastomers
- 4- PVC (polyvinyl chloride)
- 5- HDPE (high-density polyethylene)
- 6- PC (polycarbonate)
- 7- LDPE (low-density polyethylene)
- 8- Polystyrene
- 9- PTFE (Teflon)
- 10- PA (polyamides; Nylon)

These plastics are highlighted in gray in the table below for quick reference. It is noteworthy that all but one of these plastics, PTFE, are inherently radiation tolerant or are available in specifically engineered grades for enhanced radiation tolerance.

Guidelines for Component Sterilization based on Material and Process

Material	Trade Names	Radiation	Autoclave	EO Gas	Wet EO	Ethanol	Chlorine	Iodine	Peroxide	LTHPGP	Dry Heat	Ultraviolet	Microwave	Plasma	HEP Light	Food/Drug	Comments
PLASTICS																	
ABS – acrylonitrile-butadiene-styrene	Magnum, Lustran	3		2	1	2	2	1	∕								Y
ABS PC – ABS-polycarbonate alloy	Pulse	3		4													Y
Acetal copolymer, polyoxymethylene	Delrin	2	3			∕	1		∕	3							Y
Acetal + PTFE (self-lubricating for bearings)	Delrin AF	2	3							3							Cyto-toxic after machining Anti-friction, a.k.a. Lubricomp
Acrylic – PMMA – polymethyl methacrylate	Plexiglas, Kamax	2	0	5	1	∕	4	∕	∕	3	0	4					
Acrylic copolymer	Zylar, NAS 90	3	0	3		5						4					
Acrylic terpolymer	Cryolite, Cyrex	4	0	5								4					
Acrylic PC – acrylic-polycarbonate alloy	CyRex	4				5						4					
Acrylic – PVC alloy	Kydex					5			5								
EVA – ethylene vinyl acetate		4		4		∕			3	5							
EVOH – ethylene vinyl alcohol		4															
GPPS – general purpose polystyrene	Styron, Lustrex	5	0	4		∕	∕	3	∕	5	0	4					
SPS – syndiotactic polystyrene	Questra	4	5	5						5		4					
HIPS – high-impact polystyrene	Styron, Lustrex,	5	4		2	4	4	4	5	5		4					
HHCP – high-heat crystal polystyrene		5								5		4					
SAN – styrene acrylonitrile	TyriL, Lustran	4	0	4	1	∕	∕	4	5	5	0	4					
SBC – styrene butadiene copolymer	K-Resin, Styrolux	5		5		4			5	5							
SMA – styrene maleic anhydride copolymer	Dylark					5	4										
LDPE – low-density polyethylene, LLDPE	Petrothene	5	1	3		3	1	3	∕	5							Y
MDPE – medium-density polyethylene		5				4	∕	3	∕	5							F
HDPE – high-density polyethylene	Fortiflex, Marlex	4	4	5		4	∕	3	4	5				4			F
UHMWPE – ultra high mol. wt. polyethylene		3	3	5		4	∕	3	4	5							Y
MPO – metallocene polyolefin (foam)		3															
LCP – liquid crystal polymer	Vectra, Xydar	5	2			3	5										
PA – polyamides, pure and glass-filled nylon	Nylon 6,11,66,...	3	4	4	3	4	1	∕	∕	3							F
PA – polyamide, aromatic	Kevlar 29					5											
PA – polyamides, lubricated nylon	Nylatron					3	1	∕									N
PA – polyamides, oil-filled cast nylon	Nyloil					3	1	∕									Y
PAI – polyamideimide	Torlon					5											
PBI – polybenzimidazole	Celazole PBI						5										N
PBT – poly(butylene terephthalate)	Ultradur, Valox	5	1	5	4	5	2		4	5							
PET (PETP) – polyethylene terephthalate	Mylar, Dacron					5	4	5	5			4					Y
PBT – polyester alloy	Hydex 4101																Y
PC – polycarbonate	Lexan, Calibre,...	5	3	4	4	5	∕	4	4	5							F
PC – polyester alloy	Xenoy, Sabre					5	4										

Material	Trade Names	Radiation	Autoclave	EO Gas	Wet EO	Ethanol	Chlorine	Iodine	Peroxide	LTHPGP	Dry Heat	Ultraviolet	Microwave	Plasma	HEP Light	Food/Drug	Comments
PLASTICS (continued)																	
PC – polyester – PCTG alloy						5	5										
PC – SMA alloy	Arloy					4	4										
Polyester	Eastar	5		3	0									4			
PCTG – polyester		5	2	5													
PETG – polyester		2	2	1										4			
Polyimide	Kapton, Vespel	5				5	3										a.k.a. Duratron
PEI – polyetherimide	Ultem	5	5	5		4	4				4						Y
PEEK – polyetheretherketone	PEEK	5	5	5		5	1		5	5	5						Excellent chemical resistance
PPE – polyphenylene ether	Noryl, PPO, GTX	5	4			4							4				Y
PSu – Polysulfone	Udel , Ultrason	5	4	5		5	1		5	5	5						F Good chemical resistance
PES – polyethersulfone	Ultrason, Radel	4	5	5	4	5	4	4	4								Y Good chemical resistance
PPSu - polyphenylsulfone	Radel	5	5	5		5	5				4						Good chemical resistance
PPS – polyphenylene sulfide	Ryton, Techtron	5	4			4	3		2								N
PP – polypropylene	Pro-fax, Marlex	!	3	3	3	5	4	4	5	5							Y
Polypropylene (natural)		2															
Polypropylene (stabilized)		2															Y
Polyphenylene sulfide	Ryton, Supec	5				5	3		3								
Polyurethane: aliphatic		5		2	1	1	1			5							
Polyurethane: aromatic		4		2	1	1	1			5							
TPUR – thermoplastic polyurethane, rigid	Isoplast	5	1	5		4	4		4		5						
CPVC – chlorinated polyvinyl chloride	TempRite					4	5		5								N
PVC – polyvinyl chloride – Rigid	Rigid PVC	3	3	5		5	4	1	5	5							N
PVC – polyvinyl chloride – Flexible	Flexible PVC	3	5	5		5	4	1	5	5							
PVC/PVA – polyvinyl chloride/acetate		2								5							
Polyvinylidene dichloride	Saran	2		4		4	4	3	4								
FLUOROPOLYMERS																	
PTFE – polytetrafluoroethylene	Teflon, Fluon	1	3	5		5	4	4	4	5							Y
PTFE – filled	Rulon	1	3			4											Y low-friction bearing material
PFA – perfluoro alkoxy	Teflon PFA	5	4	5	4	5	4	4	5								Y
PCTFE – polychlorotrifluoroethylene	Aclar, Kel-F	4	4	3	3	5	4	4	5					5	4		
PVF – polyvinyl fluoride	Kynar, Foraflon	4	4	5													
PVDF – polyvinylidene fluoride	Kynar	5	5	5			4		5								Y
ETFE – ethylene-tetrafluoroethylene	Tefzel	5	5	5	4	4	4	4	4	5							
ECTFE – ethylene-chlorotrifluoroethylene	Halar ECTFE			5	4	4	4	4	4	5							Y
FEP – fluorinated ethylene propylene	Teflon FEP	3	4	5		5	4		4								Y

Material	Trade Names	Radiation	Autoclave	EO Gas	Wet EO	Ethanol	Chlorine	Iodine	Peroxide	LTHPGP	Dry Heat	Ultraviolet	Microwave	Plasma	HEP Light	Food/Drug	Comments
THERMOSETS																	
Phenols		5															
Epoxies		5															
Polyesters		5															
ELASTOMERS																	
Butyl	Butyl Rubber	1				4	3	3	4								
Chlorosulfonated polyethylene rubber	Hypalon	1		2	1	5	4	3	4								
EPDM –ethylene propylene diene methylene	Nordel	5				5	4	3	4								
Fluoroelastomer				2	1	5	5	5	4								
Nitrile	Nitrile Rubber	4		2		4	1	3	5								
Polyacrylic		1															
Polychloroprene	Neoprene	3		4		5	2	1	4	4							
Polysulfide rubber						5	1		2								
PVA – Polyvinyl alcohol is this an elastomer?						0											PVA is water soluble
PVC – polyol	Colorite, Everflex					5	4	5	5								
Rubber, natural		4		2	1	4	1		5								
Silicone		3	4	5		4	1		4	5	5						
Methylsilicone	Silastic			3		5											
Fluorosilicone				4		4	4	5	4								
PDMS – polydimethyl siloxane	Sylgard		3			5						5					Dow Corning type 184
Styrene-butadiene rubber		3		2		5	1	3	3								
Urethane		5															
Tetrafluoroethylene perfluoromethyl vinyl ether	Kalrez			5		5	4	4	5								
Tetrafluoroethylene propylene copolymer	Aflas			5	4	5	4		5								
TPE – thermoplastic elastomer (olefinic)	Santoprene	4	5	5		4			4		4						
Thermoplastic elastomer (polyamide)	Zytel, Pebax					5	5										
STPE – styrenic thermoplastic elastomer	C-Flex, Kraton G	4	4	5		3	4	3	4	5							
TP – thermoplastic polyester elastomer	Hytrel, Ecdel	5		4		4	2	3									
Thermoplastic polyester urethane elastomer						4	4		5								
TPUR – polyurethane thermoplast elastomer	Isoplast	4	0	4		3					4						
Thermoplastic polyether urethane elastomer						3	4		5								
COPE – copolyester ether elastomer	Ecdel	4	5	5													
CELLULOSICS																	
Cellulose esters		2								1							
Cellulose acetate	Tenite Acetate	2		1	1	1	2	2	2	1							
Cellulose acetate butyrate	Tenite Butyrate	2		V	1	1	1		3	1							

Cellulose acetate propionate		2				1		4		5								
Cellulose paper and cardboard		2								1								
Material	Trade Names	Radiation	Autoclave	EO Gas	Wet EO	Ethanol	Chlorine	Iodine	Peroxide	LTHPGP	Dry Heat	Ultraviolet	Microwave	Plasma	HEP Light	Food/Drug	Comments	
METALS																		
302, 303, 304 Stainless Steels (18-8 SS)			5	5		5	0	0	0	5	5		0					Passivate after machining
316, 316L Stainless Steels			5	5		5				5	5		0					Passivate after machining
412, 420, 440 Stainless Steels			2	5		4	0	0	0	5	5		0					
17-4 PH Stainless Steel			4	5		5	0	0	0	5	5		0					Precipitation hardening SS
Brass (unplated)										3								
Monel										5								
Aluminum (6061 alloy)										5								
Titanium (see different grades from Magellan)																		
Aluminum – 6061																		
GLASSES and CERAMICS																		
Borosilicate glass																		
COMPOSITES																		

Table Notes

Grading system: 5 = excellent, 4 = very good, 3 = good, 2 = fair, 1 = poor, 0 = failure

12345 = underline indicates that the process may only be applied one time for a short period, not repeatedly

12345V = italic indicates significant material damage may occur with increased duration, temperature, concentration or intensity

12345 = Bold indicates quarantine required before use (~ 7-14 days to desorb/outgas EO residues, for other processes times vary)

! = catastrophic failures have been reported resulting from this process

V, *V* = highly variable results, depends upon manufacturer formulation and processing, *V* = variable and degrades with increasing concentration

Gray highlight indicates the most commonly used plastics in medical devices

Radiation = ionizing radiation, which includes: Gamma radiation at recommended dosages, but may include electron-beam

Ultraviolet light at 254 nm wavelength

Wet EO = wet ethylene oxide (EO) gas

Dry Heat = typically 160-180 °C

Iodine = iodine solutions

Chlorine = chlorinated bleach solutions, typically 10% in water at room temperature, or chlorine dioxide gas

Peroxide = hydrogen peroxide

Plasma = gas plasma sterilization

LTHPGP = Low-temperature hydrogen peroxide gas plasma (Sterrad® technology)

HEP Light = high-energy pulsed light

Microwave = microwaveable

Food/drug: (Y = yes, F = food grade only, N = no) may be approved for contact with food or drugs by FDA CFR Title 21. Note that final product compliance depends upon acceptable processing and use, and may only be for specific grades of the listed material.

Notes on the use of the table: The data included in the table above were compiled from many sources. Some data are quantitative, others qualitative, some has been published under juried review, and some arises from direct experience from the author. The data are intended as a starting point and as an approximate design guideline only. For all applications, the exact material, surface characteristics, and details of the sterilization process should be defined and tested. Note also that the failure modes for each material and sterilization process can be quite different. A failure mode such as severe discoloration may cause a low rating in this table, but may be perfectly acceptable, or even desirable, in the intended application. More detailed information on each material and processing considerations, including sterilization, are included with each material listing in the Materials chapter. See the Resources section at the end of this section for detailed information.

Testing Methods (for plastics and elastomers):

In general it will be necessary to perform tests on each design and method of sterilization. Two general types of failure should be considered: (1) undesirable effects on the materials being sterilized that drive them out of design limits, or (2) failure to achieve or maintain the required sterility or asepsis.

There are many failure modes that can result from sterilization. For undesirable effects on the materials being sterilized these include dimensional changes, which can interfere with the fit and function of mechanisms and mating components, fatigue cracking, which can result from thermal cycling or chemical attack, undesirable changes in mechanical or physical properties, including reduced strength, embrittlement, changes in stiffness, changes in optical properties (e.g. loss of optical clarity), changes in molecular weight or crosslinking of polymeric materials, changes in surface chemistry and properties, spalling, crazing, or fretting of the surface, undesirable absorption, adsorption, or chemical reaction with sterilizing agents,

It is important to consider transient effects which may cause failure, specifically those that occur only during the sterilization process, such as differential thermal expansion of mating components. A common example is metal fittings in plastic components. Metal fittings generally change dimension differently than plastic, elastomeric or ceramic components, and this may cause great stress on mating components such as screws, threaded or tapered connectors, seals, etc. A tight-fitting screw, expanding more rapidly than the material it is mated with, can easily cause failure at the interface between the different materials. Also, the sterilization environment may cause transient but damaging chemical interactions between mating components.

Testing usually involves exposure of the material or device to the sterilization environment for a number of sterilization cycles. This depends upon the intended use. Single-use disposable devices may still be exposed to several sterilization cycles to amplify the effects of sterilization to determine if there exists the possibility of a failure when large numbers of the devices are sterilized and put into service. Durable or permanent devices or components which may be subjected to repeated sterilization during their service life should be tested for a larger number of cycles than is anticipated during extended service. And in all cases, the most severe sterilization conditions permissible within the process limits should be employed for testing (greatest temperature changes, radiation exposure levels, pressures, etc.)

ESCR – Environmental Stress Crack Resistance (page 3-4 of Massey book)

Yellowness index, color changes (Massey book)

Post-radiation OIT (see Massey pg 8)

PDL (Plastics Design Laboratory) Resistance Ratings Guidelines (see Massey, pg 272)

Resources

The definitive reference for the effects of the most commonly used methods of sterilization on medical and agricultural (food packaging) plastics, is “The effect of sterilization methods on plastics and elastomers, 2nd ed.”. Liesl K. Massey. ISBN 1-884207-26-X 1996, available in hard copy and CD-ROM.

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http://www.reproline.jhu.edu/english/4morerh/4ip/IP_manual/F_Disinfectants.pdf

Centers for Disease Control and Prevention website:

Appendix B: Decontamination and Disinfection:

<http://www.cdc.gov/od/ohs/biosfty/bmb15/Appendix%20B%20%20Decontamination%20and%20Disinfection.pdf>

Principles of Biosafety:

http://www.cdc.gov/od/ohs/biosfty/bmb15/BMBL%20Principles%20of%20Biosafety%20Section%203_Final%20Document.pdf