containers, thermoformed containers, tin-free steel and foil-plastic combinations.

Gaseous sterilization

When sterilization by heat is not possible, one alternative is to use a sterilizing gas. Not many gases are used in the pharmaceutical industry for sterilization and it is important to note that some of these gases are also used for disinfection (as either a liquid or a gas) under different conditions. Pharmacopoeias usually recommend the use of ethylene oxide for gaseous sterilization of pharmaceutical preparations, although other chemicals are available, such as formaldehyde, hydrogen peroxide, chlorine dioxide, peracetic acid and ozone. The chemical biocides are generally separated, according to their mode of action, into alkylating and oxidizing agents.

Alkylating gases

Some alkylating gases can permeate through many polymeric materials and are therefore not limited to just surface applications.

Ethylene oxide is widely used in pharmaceutical manufacturing but less so in hospitals. It occurs in gaseous form at room temperature (boiling point 10.7 °C) and penetrates narrow spaces well. Ethylene oxide has been shown to possess bactericidal, fungicidal, virucidal, sporicidal and protozocidal properties (Dusseau et al 2004).

The use of (LTSF) sterilization has been mentioned already. Formaldehyde is a surface sterilant only and cannot be used to sterilize occluded areas. Penetration into porous materials can be inhibited by the formation of polymers that crosslink, preventing further sterilant access (Chapter 15 provides more information).

Oxidizing gases

Oxidizing gases are relatively unstable and their decomposition can lead to microenvironments within the load that are not exposed to the full concentration of the agent.

Hydrogen peroxide gas has been shown to be effective against spores at a range of temperatures. Its action is greatest when used at near-saturation levels on clean dry surfaces and it does not leave a toxic residue (McDonnell 2007). The vapour is usually obtained via evaporation of a heated stock solution. Water condensation on surfaces that are being sterilized can reduce local concentrations of hydrogen peroxide and hence its activity; decomposition by catalytic activity and absorption by cellulosic materials (e.g. paper) can also reduce its effectiveness. The combination of hydrogen peroxide with cold plasma, cupric or ferric ions, ozone or UV has been shown to enhance activity (Dusseau et al 2004).

Ozone has been demonstrated to be an effective sterilant, but the complex control of humidity required and corrosion problems have limited its applications and it is not routinely used. Ozone as a disinfectant for water currently shows more promise and commercial systems are available for several applications.

Chlorine dioxide is a broad-spectrum biocide with a sporicidal activity and it is mainly used for the high-level disinfection of medical devices. Its applications are limited due to its effect on materials such as uncoated aluminium foil, uncoated copper, polycarbonate and polyurethane (McDonnell 2007).

Peracetic acid exists as a liquid at room temperature and is used for high-level disinfection (discussed below). Vaporized peracetic acid can be used for the sterilization of surfaces and devices, although a long contact time is required. Peracetic acid can cause corrosion of certain metals and rubbers and has low penetrating power.

Vaporized oxidizing agents are often used in combination or with plasma. Formulations also contain excipients that reduce their negative impact, such as smell and corrosiveness.

Radiation sterilization

There are two main types of radiation: electromagnetic and particulate.

- electromagnetic radiation – γ-rays, X-rays, ultraviolet (UV), infrared (IR), microwave energy and visible light
- particulate radiation – α-rays, β-rays (high-speed electrons), neutrons and protons.

Of these, only γ-rays and high-speed electron beams are used for sterilization of pharmaceutical products, since other forms of radiation have not been shown to be effective as sterilants and/or are not suitable (McDonnell 2007). Both γ- and β-rays are forms of ionizing radiation (Chapter 15 provides more information on mode of action and resistance). One advantage of irradiation is that it does not cause