Ethylene Oxide (EtO or EO) – The Future Of Gas Sterilization

Currently the overwhelming demand for EtO comes from the chemical industry, where it is a very widely used monomer. The single biggest use for EtO is in the manufacture of Ethylene Glycol which is used both directly as anti-freeze and also as an intermediate in the production of polyester (clothing) and PET (packaging). This accounts for over 99% of global EtO use.

Ethylene Oxide (EtO) has been used as a sterilant for a century. It has stood the test of time as a very effective sterilant, being good at both killing a wide range of pathogens and sterilizing the most complex shapes [1]. It continues to be the major technology for the sterilization of medical devices worldwide. Indeed, if you look at the back of packages containing devices for use in surgery some 70% contain the statement "Sterile EO" [2].

EtO is very good at reaching all parts of complicated shapes, even going through most plastics. So, long, narrow lumens and complicated shapes present no problem to EtO. For instance, a Line-Pickerill helix (1 metre stainless steel tube, with 2mm lumen open only at one end) can be readily sterilized with EtO.

EtO has no effect on the item being sterilized, so designers are not restricted in the plastics they can use, as they are when sterilizing with gamma irradiation (AAMI TIR 17 [3]).

Raw material designation	Radiation	EtO	Moist Heat	Dry Heat	Hydrogen Peroxide	Ozone
Cellulose ester	2	4	1-2	1-3	1	1-3
Cellulose, paper, cardboard	2-3	4	1-2	1-2	1	1-3
EPDM	3-4	4	3-4	2-3	2-3	2
Perfluoro alkoxy (PFA)	1	4	4	4	4	4
Polyamides (eg. Nylon)	2-3	4	1-4	1-4	3	3
Polycarbonates (PC)	3-4	4	1-3	2	4	4
Polyethylene (PE)	3-4	4	1-3	1-2	4	4
Polypropylene (PP) stabilised	2-3	4	2-3	1-3	4	4
Polytetrafluoroethylene (PTFE)	1	4	4	4	4	4
Polyvinylchloride (PVC)	3	4	1-2	1-2	4	4
Silicone adhesives	2-3	4	1-3	2-4	2	3

1 = Do not use => 4 = Completely compatible

Endoscope manufacturers typically discharge their responsibilities under ISO 17664 "Sterilization of medical devices - Information to be provided by the manufacturer for the processing of resterilizable medical devices" by specifying sterilization by EtO. Karl Storz have specifically confirmed the material compatibility of all their flexible endoscopes with the Andersen flexible chamber system[4].

Though EtO has global dominance in the sterilization of single-use devices it does not enjoy the same position in re-sterilization. Its adoption has an irregular global pattern, with widespread use in the Americas (including the USA), Middle East and Far East (excluding Japan), but less use in Europe and hardly at all in Japan. The successful adoption of EtO technology has been driven by its:

- low toxic threat
- low cost
- high effectiveness
- low environmental impact

In the UK the use of EtO has also been more widely adopted in the veterinary sector compared to human health. This appears to be primarily down to the great cost awareness in veterinary practice. Human health facilities typically make greater use of single use devices, which would make many procedures unavailable to animal owners simply due to cost.

EtO does not compete with autoclaving. Where items can be re-processed through an autoclave it will be cheaper and quicker to do that. EtO comes into its own with items that will be damaged or destroyed by autoclaving. Typically these items will contain plastic/ rubber or electrical components, such as endoscopes and various laparoscopic devices, or they contain optics or cutting/grinding edges, such as devices for ophthalmic surgery. Some hospitals also save money by routinely sterilizing procedure kits containing items such as drapes, bandages and swabs that were purchased non-sterile.

Toxicity:

The only statistically significant epidemiological study on the carcinogenicity of EtO was conducted by NIOSH (National Institute Of Safety & Health in the USA), Mortality Among Workers Exposed To Ethylene Oxide – Steenland 1991.[5] This study was updated in 2003 and covered 18,235 men and women who had worked at 14 plants (belonging to 10 different companies) from the early 1940's through to the 1980's. In 1985 OSHA lowered its 8hr TWA from 50ppm to 1ppm, meaning that this study cannot be repeated or extended. Workers in the study were exposed to tens of ppm EtO, for the duration of every working day, for tens of years.

Death rates and causes of death in the general U.S. population were compared with those in the study. The study found that overall the occurrence of cancer in the study population (that had been exposed to EtO) was **LOWER** than in the general population. The study also found that there was a trend of increased cancer incidence with increasing years of exposure. Those exposed for more than 20 years showed the same level of cancer occurrence as the general population. It is this TREND that leads NIOSH to classify EtO as a "potential human carcinogen".

There have been other studies using laboratory animals. However, the levels and modes of exposure in these studies bear no resemblance to any human activity. Consequently OSHA states that EtO "has been shown to cause cancer in laboratory animals".

In the context of a sterilization facility, using a modern EtO sterilizer, exposure to EtO will be well below even the most sever occupational exposure limits, even for the brief time the operator is in the vicinity of the sterilizer. Operators are not required to wear any personal protective equipment.

EtO is certainly a toxic gas. It is a sterilant after all. So there are maximum allowable levels of EtO in the workplace. However, it should be remembered that EtO has the lowest human toxicity of any gas used for sterilization.

	WEL – UK [6]		OSHA – USA
	8 hour	15 minute	IDLH
EtO	5 ppm	-	800 ppm
H_2O_2	1 ppm	2 ppm	75 ppm
O_3	-	0.2 ppm	5 ppm

[WEL – Workplace Exposure Limit. OSHA – Occupational Safety and Health Administration.]

Cost:

There are two aspects to this. One is the straightforward cycle cost, either in house or at a sub-contractor. The second is the cost of the time a device has to be out of commission before it can be used in the next procedure. Though it is not possible to give precise global figures on costs, EtO is cheaper than alternative low temperature technologies and sterilization cycles are now as short as 3 hours.

Contract sterilization cycles for small lots (60 litre chamber) in the UK will typically be around £100 - £150 and for traditional large chambers the prices will be even lower. In large, traditional chambers, items will be loaded on pallets and many pallets at a time go into the one chamber. Hospitals will not do enough re-sterilization to justify bringing traditional chamber technology in house. Whilst it is cost effective, cycles are slow, typically two days, and the transport time tends to mean that hospitals have to allow two weeks between

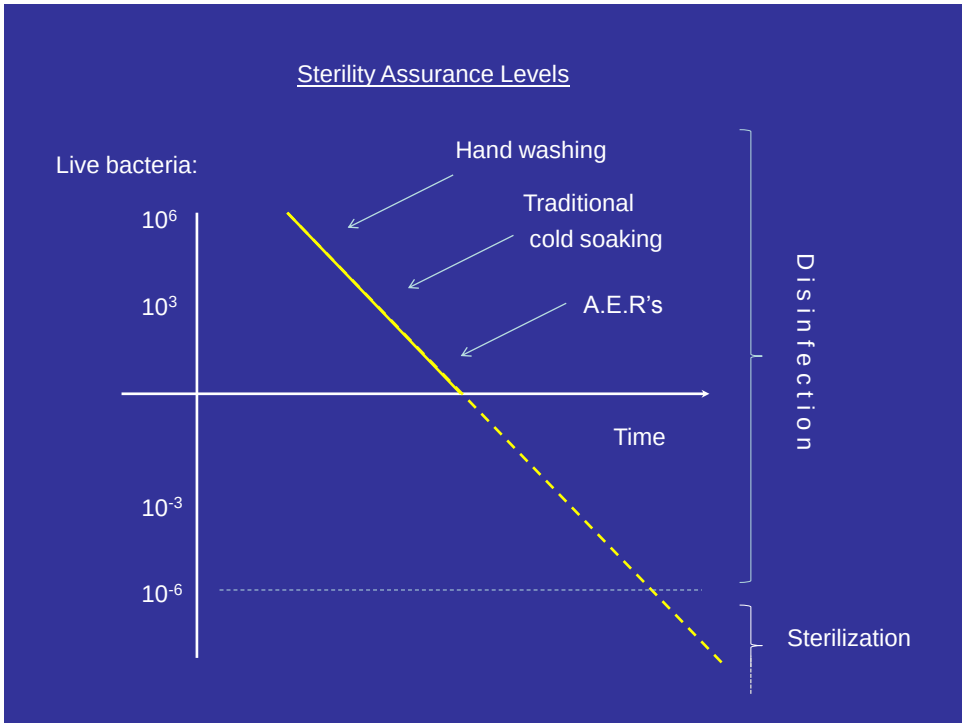
uses of each device. That can mean purchases of multiple copies of expensive devices, to support the frequency with which the relevant procedures are performed.

Technology is now available that allows EtO to be brought in house on a small scale, cost effectively. Ambient temperature cabinets are available for around £3,500, with a consumable cost of around £15 per cycle. These will run overnight. There are also heated cabinets that will run a complete cycle in 3½ hours, which cost around £15,000, with the same consumable cost of £15 per cycle.

Most items will be safe to use on the patient immediately after they come out of the sterilizer, as modern EtO sterilizers include an aeration phase at the end of every cycle. However, it is a feature of EtO that it is absorbed by many materials, particularly soft plastic, and some devices may need further aeration before they can be re-used.[7] Where the device has EtO absorbing material that will come into contact with sensitive tissue (GI tract, the eye, wound or surgical site) the traditional guidance has been to aerate at 20°C for 24 hours. This extended aeration is considerably accelerated in a heated cabinet, giving users the ability to use the most effective sterilant and re-use all their delicate and expensive equipment again the same day.

Effectiveness:

All EtO cabinets will sterilize an item with a degree of overkill. Heated EtO cabinets will deliver the 10^{-6} SAL (Sterility Assurance Level) required by BS EN 556-1:2001.[8] This is the standard applicable to the sterilization of medical devices intended for human use. This is the level of sterility achieved by autoclaves and should not be confused with disinfection.



Sterility assurance levels and the difference between disinfection and sterilization.

Some devices, e.g. flexible endoscopes, have historically been cold soaked. Much work has gone into improving the performance of soaking technologies, both in terms of the level of disinfection achieved and in terms of the damage caused to the items being treated. The result has been Automated Endoscope Reprocessors (AER's) that achieve consistently high levels of disinfection with little or no damage to the scope. Even AER's do not kill all the micro-organisms on a device, and the term disinfection is widely used to make this clear.

Disinfection presents three problems. 1) There are stringent requirements on the water used for rinsing after disinfection, with the costs of testing and control that go with that. 2) The items being soaked are not in sterile packaging. The British Society for Gastroenterology (BSG) has recommended for human use that "All endoscopes must have been exposed to a full decontamination cycle not more than 3 hours prior to use". This

poses significant planning and operational challenges, whilst not delivering a sterile device to the surgeon. 3) Disinfected endoscopes may still transfer infection, so endoscopes will need periodic sterilization even if they are not sterilized between each patient.

EtO has also proven to be especially effective at denaturing background DNA. This has made it the method of choice for forensics companies, ensuring their consumables, used in crime-scene forensic sampling kits, are free of any DNA that can be profiled.[9]

Environment:

The exhaust ETO is vented to the outside where there are virtually no restrictions. In the USA there are no federal restrictions provided annual emissions are less than 1 ton.[10] Small in house cabinets will emit nowhere near this level of EtO. However, large traditional chambers used by contract sterilization companies will have to employ abatement technology. There are local regulations in some districts in the USA, which require more than 99% of the EtO used each cycle to be absorbed rather than emitted to atmosphere. This applies regardless of the amount of EtO used per cycle. So the 1% emitted from large chambers will exceed the total usage per cycle in small chambers. Nevertheless, it has driven the development of small abator technology for that has found a use outside these regulated districts in the USA.

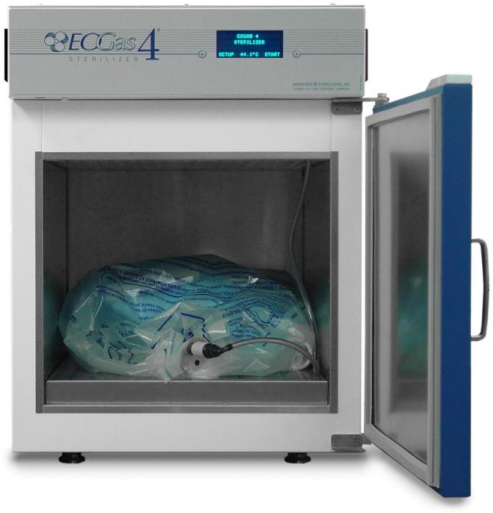
Customers may choose to adopt EtO abator technology either because they wish to be seen to be using the best available technology, or for more practical reasons. In some establishments the EtO sterilizer is not situated close to a suitable outside wall. Here it can be convenient to release the exhaust gas into the common venting system to be ducted up for emission from the roof. In this case absorbing more than 99.9% of the EtO in the exhaust, before releasing it into the common ducting system, ensures that any escape on the way to the roof cannot generate levels of EtO in the workplace that pose any risk.

The freedom to emit EtO in the UK arises because it is not a greenhouse gas (Kyoto Protocol[11]), it is not a volatile organic compound (VOC, Geneva Protocol[12]), it is not an Ozone depleter (Montreal Protocol[13]) and EtO is not covered by the Pollution Prevention and Control Act 1996, which is the UK implementation of the EU Council Directive 96/61/EC[14]. This makes sense because EtO is rapidly absorbed by water in the environment and degrades either by conversion to ethylene glycol or by alkylating available organic material.

In short by virtue of the ability of very small amounts of EtO to achieve high levels of sterility and then to degrade in the environment, EtO is an environmentally friendly, green product.

Adoption:
There are five scenarios driving the adoption of in house EtO for re-sterilization:

- Reduced damage:- Products remains compared to sterilization with H_2O_2.
- Surgical consumables cost:- Items may be purchased unsterile and then sterilized prior to use.
- True sterilization:- Sterilize devices that have traditionally been disinfected (eg cystoscopes)
- Lower cost sterilization:- Compared to traditional EtO cabinets or H_2O_2 sterilizers.



So, Ethylene Oxide has the effectiveness and cost competitiveness to address a range of operational issues, as well as the green credentials to satisfy the modern marketplace. No wonder its global fan base continues to grow.

EOGas Series 4 sterilizer, capable of sterilizing in just 3 hours.

References:-

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5. Steenland et al. “Mortality among workers exposed to ethylene oxide.” New England journal of Medicine 1991.
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14. Council Directive 96/61/EC concerning integrated pollution, prevention and control.