Scottish Health Technical Memorandum 2010

(Part 5 of 6)

Good practice guide

Sterilization

NHS in Scotland, HEEU, August 1999

Preface

SHTM 2010 gives guidance on the choice, specification, purchase, installation, validation, periodic testing, operation and maintenance of the following types of sterilizer in use in the National Health Service:

a. clinical sterilizers:

   (i) high-temperature steam sterilizers used for processing porous loads (including instruments and utensils wrapped in porous materials);

   (ii) high-temperature steam sterilizers used for processing aqueous fluids in sealed containers;

   (iii) high-temperature steam sterilizers used for processing unwrapped solid instruments and utensils;

   (iv) dry-heat sterilizers (hot-air sterilizers);

   (v) low-temperature steam (LTS) disinfectors and low-temperature steam and formaldehyde (LTSF) sterilizers;

   (vi) ethylene oxide (EO) sterilizers;

NOTE: Despite their name, LTSF sterlizers are disinfectors.

b. laboratory sterilizers:

   (i) high-temperature steam sterilizers used with one or more specialised operating cycles;

   (ii) culture media preparators.

No guidance is given on sterilization by irradiation, hydrogen peroxide, gas plasma or filtration. Users who wish to employ these processes bear the responsibility of ensuring that the validation procedures comply with the principles outlined in Part 3 of this SHTM and that the intended operating procedures will ensure an efficacious process for the different types of load.

This SHTM is intended primarily as a guide for technical personnel, whether specialists in sterilizers and sterilization procedures or those responsible for maintenance and testing. It is also intended for those responsible for the day-to- day running of sterilizers, and will also be of interest to supplies officers, architects, estates managers and others in both the public and private sectors.

Detailed information on the planning and design of a sterile services department, including the level of provision of sterilizers, is given in Scottish Hospital Planning Note 13; *Sterile services department*. Guidance for laboratory installations can be found in Scottish Hospital Planning Note 15; *Accommodation for pathology services*.

Although this edition of SHTM 2010 reflects established sterilizer technology, it is recognised that considerable scope exists for the utilisation of emerging technology in the management of sterilizers. This will be kept under review with the aim of introducing recommendations for such technology at the earliest opportunity so that the procedures essential for the efficient, safe and effective operation of sterilizers can be optimised.

Most of the British Standards for sterilizers which were applicable at the time of the last edition of this HTM, in 1980, have been either withdrawn or radically revised. Some of them, in turn, are now being replaced by European Standards which will be published during the currency of this edition of SHTM 2010. Some of these European Standards support new European Union Directives on medical devices which will have a major impact on sterilization. Where practicable the information in this SHTM has been aligned with existing or anticipated standards and advice is offered where no standard has yet been formulated.

The sterilizers described in this SHTM may not be suitable, without modification, for safely processing articles infected with Hazard Group 4 pathogens nor agents, such as those associated with transmissable spongiform encephalopathies, which are unusually resistant to sterilization. Design considerations for sterilizers intended to process articles infected with such organisms are discussed in Part 2.

This part of SHTM 2010 contains detailed supplementary information that expands upon the guidance given in Parts 1 to 4 and should be read in conjunction with them.

NOTE: Information about Hazard Groups may be found in the HSC document ‘Categorisation of pathogens according to hazard and categories of containment’ (second edition 1990) compiled by the Advisory Committee on Dangerous Pathogens.

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Section A

The lethality of heat sterilization processes – the F_0 concept

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A1. Introduction

A1.1 There are several, well established, time temperature relationships for thermal sterilization methods which are regarded as equally acceptable (see Part 3 of this SHTM, Table 8). Clearly temperatures other than those shown, when maintained for an appropriate time, will also be capable of producing a sterile product.

A1.2 For a moist heat sterilization process, we can expect a particular time at a particular temperature to have a predictable lethal effect against a standardised population of organisms. If we choose particularly resistant organisms and assume they are present in numbers in excess of that likely to be encountered in real product we can define standard exposure conditions which will always yield a sterile product in a correctly operated sterilizer. Actual exposures can then be related to these standard exposure conditions.

For example, in the laboratory it is possible to produce conditions where the time to attain a pre-selected sterilization temperature, and the time to cool to ambient temperature after sterilization, is so short that it may be disregarded: a so-called “square wave exposure” system. This will enable very accurate determinations of the thermal resistance of micro-organisms under well defined conditions, and from several such determinations at different temperatures an accurate determination of the change in thermal resistance with temperature to be made.

Operational sterilizer cycles do not produce this rapid heating and cooling but have relatively slow temperature changes. The product is thus exposed to temperatures somewhat below the chosen sterilizing temperatures for considerable periods. It is apparent that there will be some lethal effect on micro-organisms during the heating and cooling phases of any particular sterilization cycle since microbial death occurs over a wide range of temperatures, albeit at different rates.

The F_o concept recognises this and allows us to take account of the lethality obtained during the heating and cooling phases.

A1.3 For heat sensitive products it is desirable to minimise the heat treatment given to the product and reduce the energy input to a level which, while providing adequate assurance of sterility, will minimise the degradation of the product. Because the F_o concept allows us to take account of the inactivation of micro-organisms throughout the cycle, not just during the sterilization hold period, we can thus obtain a cycle with the required lethality but with minimum thermal degradation.

A1.4 In summary, optimisation of thermal sterilization processes may be achieved by means of the *F* method which uses a knowledge of the lethality of the particular process at different temperatures to assess the overall lethality of the cycle and express this as the equivalent exposure time at a specified temperature.

A1.5 *F* is defined as the equivalent time in minutes at 121.1°C to produce a given sterilization effect.

A1.6 Where the specified temperature is 121.1°C (250°F) and the Z value is 10°C the term F_0 is used.

The F_0 value of a saturated steam sterilization process is the lethality expressed in terms of the equivalent time in minutes at a temperature of 121ºC delivered by that process to the product in its final container with reference to micro-organisms possessing a Z value of 10.

The total F_0 value of a process takes account of the heating up and cooling down phases of the cycle and can be calculated by integration of lethal rates with respect to time at discrete intervals.

A1.7 The F_0 method may be used for assessment, or control, of processes where difference in temperature is the only factor influencing the efficacy of the cycle. For example, it may be applied to the steam sterilization of aqueous fluids in sealed containers but it is not applicable to steam sterilization of porous loads where air removal is also a key factor and failure to achieve direct contact with Dry Saturated Steam can lead to failure, regardless of whether the required temperature was achieved within the load.

A1.8 Similar concepts are also used for dry heat sterilization processes and for depyrogenation by exposure to dry heat.

A1.9 There are a number of pre-requisites which it is necessary to consider before the use of the F_0 method is appropriate. These include:

- the efficacy of the sterilization process under consideration is dependent only on temperature eg. air removal is not critical. Thus in a porous-load steam sterilizer where impaired air removal can allow air to persist in random locations throughout the load, and where it may be present in sufficient quantity to impair sterilization, the use of the F_0 method for cycle control or monitoring is inappropriate;
- the sterilizer to be used has cycle control which is adequate to ensure that production cycles consistently reproduce the conditions established during validation. F_0 monitoring of a process may not be used to justify the use of a sterilizer which demonstrates excessive temperature variation within the load or poor reproducibility from cycle to cycle etc;
- temperature profile studies/validation studies have been conducted to establish the uniformity of conditions throughout load and to identify the location of those parts of the load which are slowest to heat up and fastest to cool down;

- the loading composition and pattern of production cycles is controlled within the limits established during validation to ensure that the results obtained remain valid;
- production controls and bioburden studies are adequate to maintain a known, low level, of microbial contamination and the thermal resistance and temperature dependence (D and Z values respectively) of the most resistant contaminant(s) are known or the assumed values are in accordance with the Pharmacopoeial recommendations.

A2. Fundamental concepts

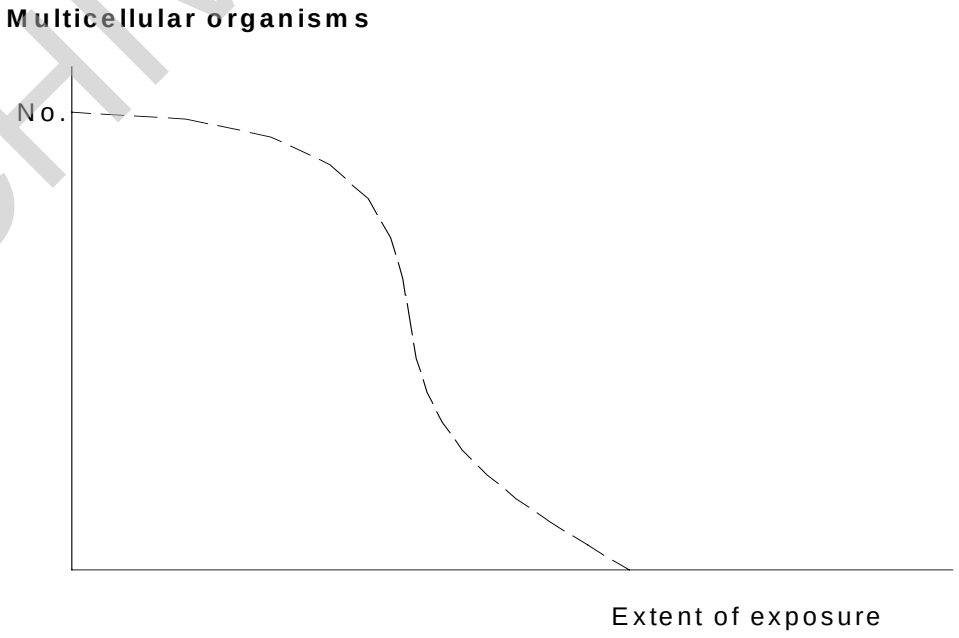
A2.1 In order to use the F_0 concept correctly it is important to understand the facts, definitions and assumptions on which the model is based. It has become common place to use certain functions and terms in the analysis and interpretation of data on the effect of physical or chemical stress on microbial survival. These terms are discussed below.

How microbes die: the logarithmic order of death

A2.2 Organisms which die as a result of an imposed stress die in an orderly, and predictable, manner. This can be represented as survivor curve, showing the number of organisms still living at various times after the beginning of exposure to the stress condition.

A2.3 The order of death is, in principle, the same for all multicellular organisms. The survivor curve remains constant for as long as individuals can recover from that length of exposure; then as the first individuals die, the frequency of death rapidly increases until only a few very resistant organisms remain, and they succumb shortly after the majority of the population (see Figure A1). In a unicellular organism the individual is dead when a single cell dies, whereas in multicellular organisms the death of one cell is not likely to kill the individual. The multicellular organism will survive until enough cells have been killed to cause death.

Figure A1: Arithmetic survivor curve for multicellular organisms

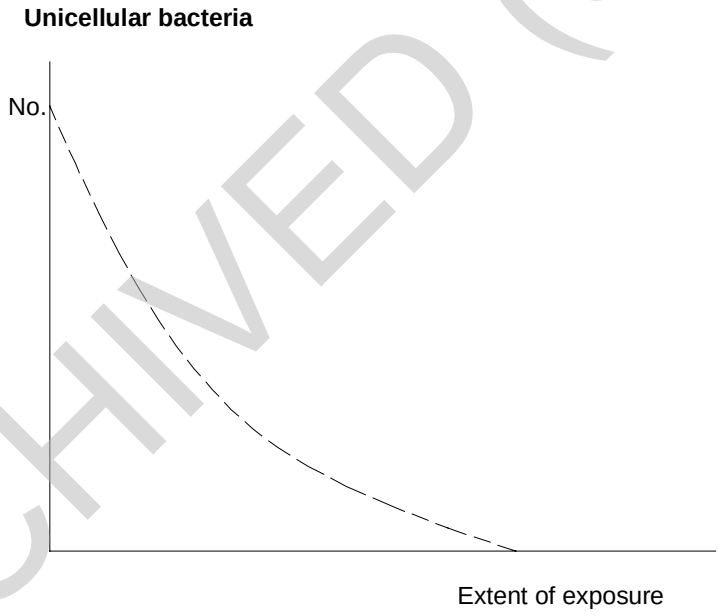


A2.4 Whichever multicellular organisms are tested, for example insects or plants, and whatever the lethal stress, the survivor curve remains essentially the same. This was accepted as universally true for all organisms until the early 1900s when workers such as Harriet Chick [see Chick (1908)] showed that in an homogeneous culture of a single strain of bacteria the cells died at a constant rate when exposed to a particular lethal stress.

A2.5 It was apparent that these bacteria were dying in a manner which was somewhat unexpected. This may be illustrated by taking as an example the survival of microbial spores subjected to heat stress. An experiment may be devised in which all factors other than the heating time are held as constant as possible. If a number of biological indicators, each bearing a known number of bacterial spores, are subjected to a thermal sterilization process, at a predetermined temperature for various increments of exposure time, and then the survivors on each indicator enumerated, the data obtained shows the number of colony forming units remaining viable after each exposure time.

A2.6 A survivor graph can be prepared showing the number of survivors as a function of the length of heating time. Both the number of survivors and the time may be plotted on an arithmetic scale (see Figure A2).

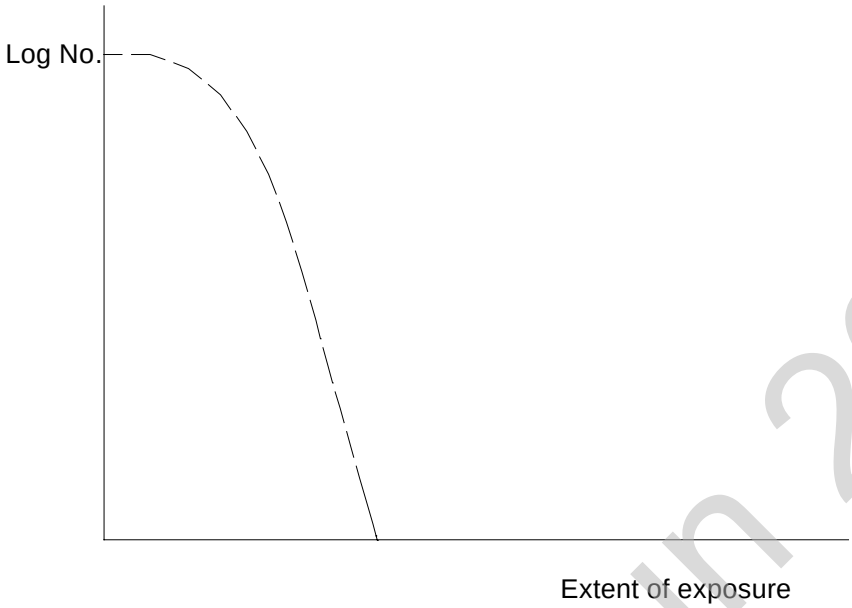
Figure A2: Arithmetic survivor curve for unicellular bacteria



A2.7 Alternatively the number of survivors may be plotted on a logarithmic scale as a function of time on the arithmetic scale, which is referred to as a semi-log survivor curve (see Figures A3 and A4). While both the arithmetic and semi-log survivor curves accurately represent the death of bacteria the latter is more useful in sterilization studies where interest is concentrated on the rate of destruction as the number of survivors approaches zero.

Figure A3: Semi-log survivor curve for multicellular organisms

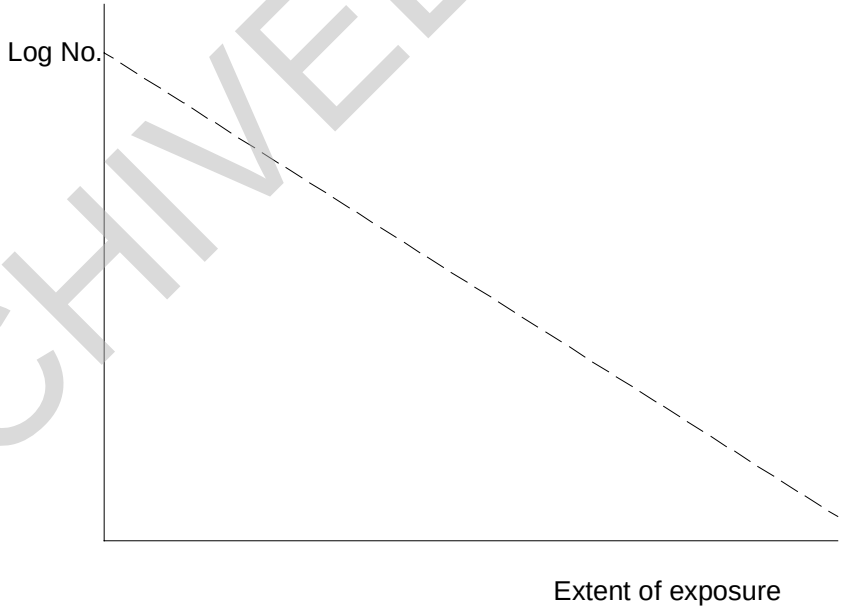
Multicellular organisms



A2.8 It is usual to use the latter approach since in sterilization studies we are interested in the rate of destruction as the number of surviving micro-organisms approaches zero, which is best shown using a logarithmic plot.

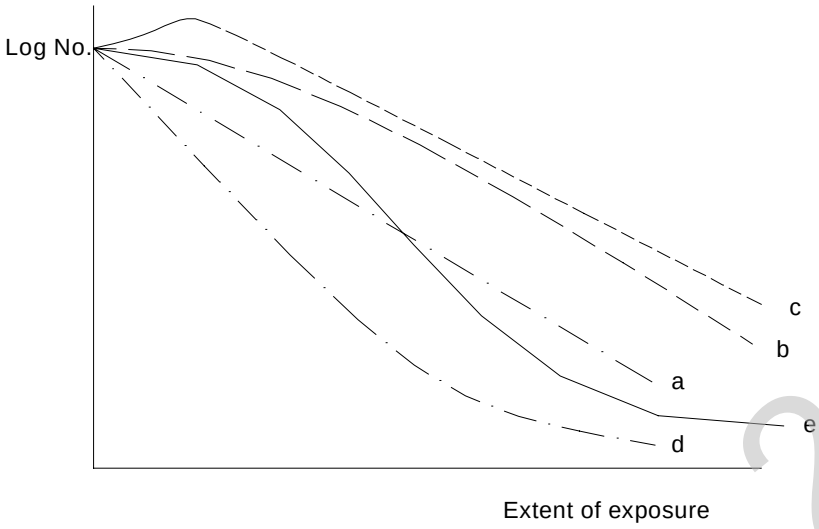
Figure A4: Semi-log survivor curve for unicellular bacteria

Unicellular bacteria



A2.9 Experience has shown that the semi-log survivor curve for heat stress often approximates to a straight line for part or all of the survivor curve. However there are many recorded instances where deviations from the “ideal” straight line condition occur (see Figure A5).

Figure A5



Microbial survivor curves showing typical deviations from the linear model; curve **a** is a theoretical linear survivor curve; curve **b** shows an initial "shoulder" followed by a linear survivor curve; curve **c** shows an initial increase in count, "activation", followed by a linear survivor curve; curve **d** shows an initial linear survivor curve followed by a decreasing rate of kill, "tailing"; curve **e** shows the sigmoidal survivor curve often encountered in experimental determinations.

Conditions resulting in a non-logarithmic order of death

A2.10 Typical survivor curves for bacterial spores exposed to moist heat sterilization processes are shown in Figure A5 in which the logarithm of the number of surviving organisms is plotted against time and various types of response are illustrated:

- *Curve a* – exponential – constant fraction of the population is inactivated per unit time;
- *Curve b* – shows an increasing death rate after an initial period where there was little or no inactivation – a "shoulder";
- *Curve c* – initial activation (increase in population) followed by a constant death rate;
- *Curve d* – decreasing death rate with a low number of highly resistant organisms surviving for a prolonged period – "tailing";
- *Curve e* – a sigmoidal survivor curve of the type frequently encountered in experimental determinations of resistance. This type of survivor curve may be regarded as a composite of elements of the survivor curves described above.

Factors influencing the nature of the survivor curve

A2.11 There are a number of factors which have a significant effect on the nature of the survivor curve. Workers such as Moats *et al* (1971) have discussed these factors in detail. Some of the key factors can be summarised as follows:

- *Growth index*. During recovery there are many instances when not all viable spores will germinate and outgrow within a short time period. The percentage of those present which do germinate and grow immediately on incubation is referred to as the growth index. The growth index varies both with the species of bacterial spore and the cultural conditions in which it was grown and is to be recovered. It may be as high as 100%,for example for Bacillus subtilis, but may be as low as <1%, for example for Bacillus stearothermophilus. Sublethal heating may increase (activate) or decrease (deactivate) the growth index and give rise to non-linear survivor curves. [see Favero (1967), Finley and Fields (1967)] The interaction of activation and inactivation on the thermal treatment of heat resistant dormant spores of B stearothermophilus can be described mathematically. [see Shull *et al*. (1963)]
- *Cell clusters*. The usual method of counting the number of surviving bacteria is by the plate count method which gives the number of colonies developed from a known volume of suspension inoculated onto the surface of solid growth medium. The number of colonies is equal to the number of bacteria present only when each colony arises from a single cell.

  When the cells are in clusters, for example Staphylococcus spp., or in chains, for example Streptococcus spp., one colony may represent a large number of cells. All the time there are one or more surviving cells within the aggregation a colony will be formed and death therefore becomes evident only when the last cell is dead. Such clusters “die” like multicellular organisms and show convex survivor curves (see Figures A3 and A5, curve b).
- *Cell age*. It has been demonstrated that young cells, that is, the exponential growth phase of a culture, are more susceptible to both chemical and physical stress than old cells from the stationary phase of a culture. Furthermore if old cells are transferred to a new environment they do not all begin to grow at the same time and a culture develops in which both old and young cells coexist leading to heterogeneous resistance and concave survivor curves (see Figure A5, curve d).
- *Mixed populations*. Where more than one strain or species is present, with different resistances to the lethal stress being imposed, a non-linear survivor curve, typically of concave form, will arise (see Figure A5, curve d).

Factors influencing the heat resistance of spores

A2.12 Any assessment of thermal resistance of micro-organisms must involve consideration of those factors which may affect the thermal resistance.

A2.13 These factors include the species and strain of organisms to be considered; its physiological state, which will in part depend on its immediate cultural history, the manner in which it is presented to the sterilization process, for example the suspending menstruum; and the recovery conditions which are used in an attempt to grow the organism after exposure to the process; as well as the exposure conditions used, for example whether dry heat or moist heat (direct contact with dry saturated steam or being in an aqueous solution) was used, and the exposure temperature. [see Russell (1971).]

A2.14 The nature of the product also affects the thermal resistance of contaminating organisms; the protective effects of various salts and carbohydrates in solution are well documented in the literature.

A2.15 The influence of changes in the manufacturing environment and/or process on the nature and extent of contaminating micro-organisms must also be considered.

Treatment of sterilization-process microbial survival data

A2.16 A mathematical approach to the resistance of bacteria to thermal death is required to allow calculation of equivalent lethality. Two factors need to be considered; the thermal resistance of the micro-organism at a particular temperature and the change in that resistance which occurs with changes in temperature.

These two factors are analogous to the rate constant and temperature coefficient of a chemical reaction, respectively.

A2.17 Spore inactivation in moist heat may be considered as a monomolecular first order reaction, that is where the rate of reaction is governed by the concentration of the reactant, in this case the bacterial spores.

This may be expressed as

$$\frac{dN_a}{dt} = k\,C_a$$

Where t = time,

C_a = spore concentration

k = a reaction rate constant at constant temperature

Then $(\log C_a^0 - \log C_a) = k\,(t - t^0)$

where the superscript 0 indicates initial conditions.

A2.18 A semi-logarithmic plot of concentration versus time will yield a straight line of slope k. k has dimensions of time^{-1}. The negative reciprocal of the rate constant k is equivalent to the number of minutes required to inactivate 90% of the organisms present, that is a 1 log reduction. This value is referred to as the D value and, as stated, mathematically it is inversely proportional to the inactivation rate constant k.

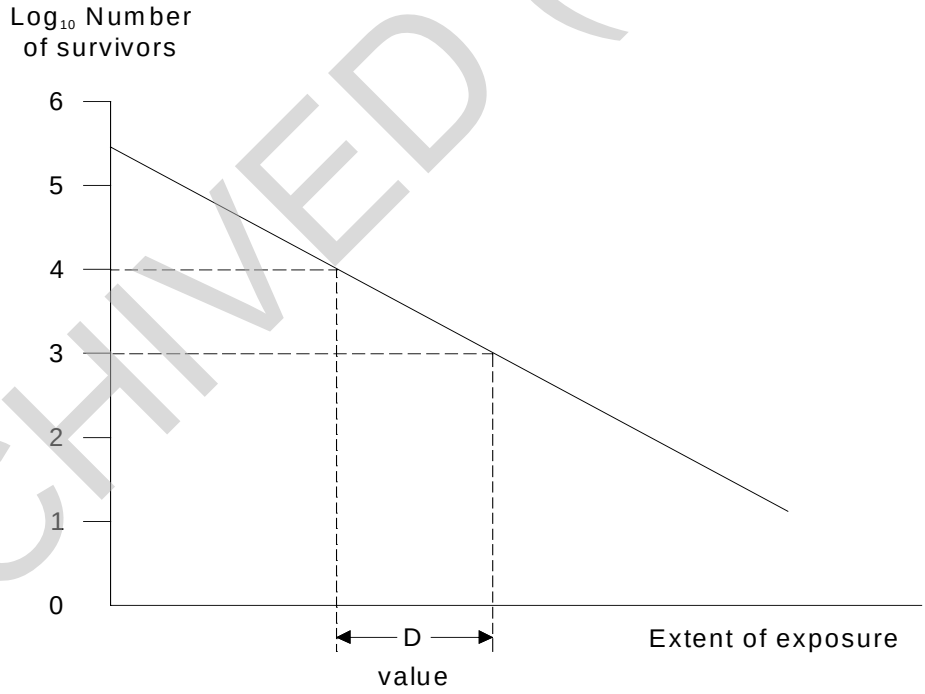
$D = 2.303 / k$.

Decimal reduction value (D value)

A2.19 The D value is used as a measure of the resistance of a defined micro-organism to a defined sterilization process. It is a convenient way to describe the slope of a linear semi-log survivor curve.

A2.20 More particularly it may be defined as the extent of exposure, under stated conditions, necessary to produce a 90%, or 1 log, reduction in the bacterial population (see Figure A6). It is usually stated in minutes, except for sterilization processes using ionising irradiation where it is given in kiloGreys (units of absorbed radiation dose).

Figure A6: Decimal reduction value



A2.21 For moist heat sterilization processes it is often given a subscript to indicate the temperature at which it was determined, for example D_{121}. Although this in itself is insufficient definition of the conditions under which the determination was made to allow valid comparison.

A2.22 The D value is highly specific to the experimental conditions under which it was determined. Even apparently minor changes in experimental procedure,

for example incubation temperature, recovery medium can have a dramatic effect on the apparent D value.

A2.23 The D value is only relevant to the survivor curve when the survivor curve is truly a straight line over the range of population values of interest, including the "probability" zone.

A2.24 It is not necessary to construct a survivor curve to determine D value The determination may be done by a replicate unit method involving fractional-unit- negative (FN) data. A number of replicates are heated for a certain time and the number viable and the number sterile are determined. [see Pflug and Schmidt (1968).]

Then where r = total number,
p = growth,
q = sterile,
U = time in min,
N_0 = initial population per replicate unit
N_U = population per replicate unit after time U,

then

$N_U = \log_n(r/q) = 2.303 \log (r/q)$

and

$$D = \frac{\textit{duration of treatment}\,(\min)}{\log \textit{initial no} - \log \textit{final no of spores}}$$

$$= \frac{U}{\log N_o - \log N_U}$$

The temperature dependence of resistance

A2.25 A common measure of the temperature dependence of a chemical reaction is the Q_{10} value. This is defined as the change in reaction rate constant k for a 10°C change in temperature:

$$Q = \frac{k^{(T + 10^{\circ} C)}}{k_T}$$

A2.26 For most chemical reactions Q_{10} has a value of about 2, but for spore inactivation in moist heat $Q_{10} \approx 10$ to 18 and for spore inactivation in dry heat $Q_{10} \approx 2.2$ to 4.6.

A2.27 Other measures of temperature dependence include the Arrhenius equation;

$$k = A \exp (-E_A(RT)^{-1})$$

Where k = the reaction rate constant;
A = the frequency factor;
E_A = the activation energy;
R = the universal gas constant;
T = the absolute temperature.

A2.28 However, the temperature dependence of reaction rates for spores is generally expressed as a Z value,

Where $$Z = \frac{\log Q_{10}}{10}$$

or $$Z = 2.303 RT^2 E_A^{\ 2}$$

Z value

A2.29 The *Z* value is a measure of the change of inactivation rate with temperature. It is the slope of a plot of *D* value on a logarithmic scale against temperature on an arithmetic scale (see Figure A7).

A2.30 The *Z* value allows comparison of the lethal effect of heating at different temperatures. [See Bigelow (1921).]

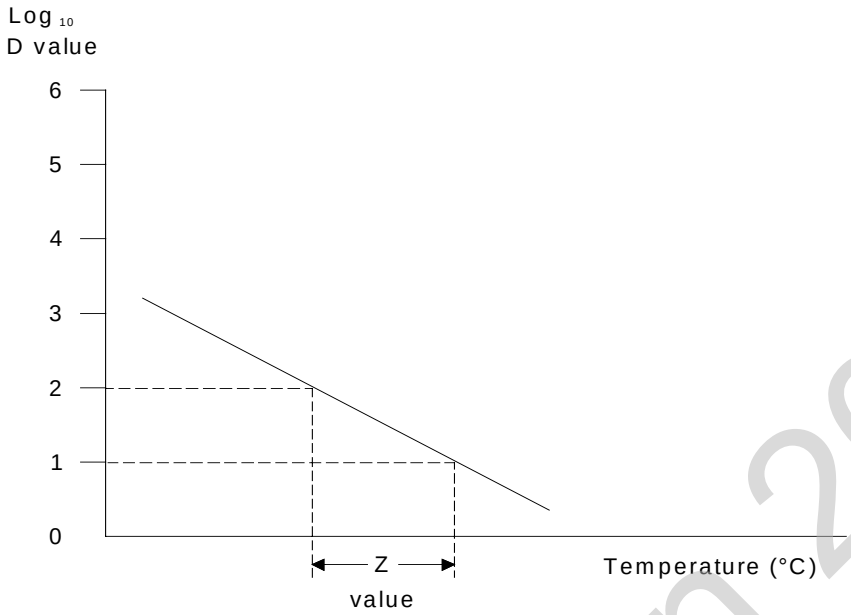
A2.31 As originally defined *Z* is numerically equal to the number of degrees Fahrenheit change in temperature required to reduce the *D* value by 90%, or 1 log. Considerable confusion, and error, can be caused where the temperature scale used is not specified. Although values are now usually given in °C care must be taken when using published data, for example from the official compendia, to note whether the *D* value is quoted in °F or °C.

A2.32 The mathematical relationship with the D value can be expressed as:

$$\log D_2 - \log D_1 = \frac{(T_1 - T_2)}{Z}$$

A2.33 It should be noted that, the greater the *Z* value, the greater the increase in temperature which is required to give a tenfold decrease in *D* value. Hence the assumption of a *Z* value higher than in fact exists will give an additional margin of safety. The *Z* value assumed for most thermophiles, such as Bacillus stearothermophilus, is 10°C.

Figure 7: Thermal resistance curve



A2.34 The straight-line relationship holds good only over a limited temperature range for an homogenous culture of a single strain of micro-organisms. Mixed cultures give a non-linear relationship, but in practice one sub-population, either by virtue of its resistance or its prevalence, will be controlling with regard to attainment of sterility.

Lethal rates

A2.35 The usefulness of the temperature dependent model lies in being able to calculate the lethality over a range of temperatures, which will include those experienced during heating-up and cooling-down of a load in a steam sterilizer.

A2.36 The relative lethality at a temperature, T_{exp}, compared to the known lethality at a particular reference temperature, T_{ref}, is dependent on the *Z* value.

Thus, the lethality L is given by the equation

$$L = 10^{(T_{exp} - T_{ref}) Z^{-1}}$$

Lethality factors for any temperature deviation from the reference temperature and for any *Z* value can be calculated using this formula (see Table A1).

A2.37 A new variable *F*, the thermal death time can be defined. The change in *F* with temperature is analogous to the change in thermal resistance (*D* value)

with temperature and both are dependent on the *Z* value. Plots of log *D* versus temperature and log *F* versus temperature both have slope Z:

$$\frac{D_T}{D_{121}} = \frac{F_T}{F_{121}} = 10^{(T-121)/Z}$$

F value

A2.38 The *F* value expresses heat treatment in terms of the equivalent effect of a stated time at some stated temperature for a particular Z value, that is to say that the *F* value is the equivalent time in minutes at 121.1°C (250°F) for an organism of specified *Z* value.

A2.39 F_0 is the *F* value when *Z* is 18°F (10°C):

$$F_0 = \sum 10^{(T-121)/Z} \Delta t$$

where t is the chosen time interval, and T is the temperature in the container.

NOTE: For dry heat *F* values, *F* is equal to the time in minutes at 176°C (350°F).

Table A1: Lethality factors for a Z value of 10°C

Temperature difference °C	Lethality factor minutes*	Temperature difference °C	Lethality factor minutes*
-20.0	0.0100	+20.0	100.000
-19.0	0.0126	+19.0	83.180
-18.0	0.0159	+18.0	66.070
-17.0	0.0200	+17.0	52.480
-16.0	0.0251	+16.0	41.690
-15.0	0.0316	+15.0	31.620
-14.0	0.0398	+14.0	25.120
-13.0	0.0501	+13.0	19.950
-12.0	0.0631	+12.0	15.850
-11.0	0.0794	+11.0	12.590
-10.0	0.1000	+10.0	10.000
-9.0	0.1259	+9.0	8.318
-8.0	0.1585	+8.0	6.607
-7.0	0.1995	+7.0	5.248
-6.0	0.2512	+6.0	4.169
-5.0	0.3162	+5.0	3.162
-4.5	0.3548		
-4.0	0.3981	+4.0	2.512
-3.5	0.4467		
-3.0	0.5012	+3.0	1.995
		+2.8	1.905
-2.5	0.5623	+2.6	1.820
		+2.4	1.738
		+2.2	1.660
-2.0	0.6310	+2.0	1.585
		+1.8	1.514
-1.5	0.7079	+1.6	1.445
		+1.4	1.380
		+1.2	1.318
-1.0	0.7943	+1.0	1.259
		+0.8	1.202
-0.5	0.8913	+0.6	1.148
		+0.4	1.096
		+0.2	1.047
0.0	1.0000	0.0	1.000

Lethality L is given by $L = 10^{(T_{actual} - T_{reference}). Z\text{-}1}$

* Lethality factor is given in minutes equivalent at the reference temperature.

A3. Sterility

A3.1 In order to utilise the F_0 method it is first necessary to decide on the extent of treatment which will be necessary to provide the required level of assurance that the product is sterile. Several different definitions are in common use.

Sterility assurance

A3.2 If the survivor curve is extrapolated beyond $\log_{10}0$, that is one surviving organism, we reach a region of "probability" of finding a single surviving organism. For example at $\log_{10}[-1]$ we expect to find, not 0.1 organisms surviving in every sample but, one in every ten samples with a surviving micro-organism.

We can thus determine from the survivor curve a theoretical probability of any one unit of product being non-sterile.

A3.3 The European standard, EN 556, in common with a definition in the *European Pharmacopoeia*, states that a product may be regarded as sterile when the theoretical level of not more than one micro-organism is present in 1×10^6 sterilized units of the final product.

A3.4 This calculation may be based on data, obtained by investigation, on the extent and resistance of microbial contamination immediately prior to sterilization (the Bioburden) or on a theoretical contamination of 10^6 micro-organisms per unit of product presumed to be of a type having known high resistance to the process, for example bacterial spores. In the latter case the cycle is often referred to as a "12D" or "overkill" cycle and was first proposed by Esty and Meyer (1922) for processing low-acid canned food products.

A3.5 The *British Pharmacopoeia* in Appendix XVIII 'Methods of Sterilization' states: "For aqueous preparations sterilized by heating in an autoclave the preferred combination of temperature and time is a minimum of 121°C maintained throughout the load during a holding period of 15 minutes." However, it goes on to say: "Other combinations of time and temperature may be used provided that the process chosen delivers an adequate level of lethality when operated routinely within the established tolerances."

A3.6 In Annex 2, 'Guidance on application of the F_0 concept to aqueous preparations', the British Pharmacopoeia suggests that "in general for aqueous preparations a microbiologically validated steam sterilization process that delivers, in total, an F_0 value of not less than 8 to every container in the load is considered satisfactory".

A3.7 In certain circumstances, however, use of a steam sterilization process that delivers, in total, an F_0 of less than 8 may be considered justifiable, for example where the product is especially heat sensitive. The nature of processes delivering an F_0 of less than 8 is such that great care must be taken in order to ensure that adequate assurance of sterility is consistently achieved. It is necessary not only to validate the process microbiologically but also to perform continuous, rigorous microbiological monitoring during routine production to demonstrate that the microbiological parameters are within established tolerances so as to give a theoretical level of not more than one living micro-organism per 10^6 containers in the final product.

A3.8 The *European Pharmacopoeia* also states that the recommended method for parenteral products is moist heat sterilization at a minimum of 121°C maintained throughout the load for a minimum of 15 minutes. Other time temperatures can be used but the crucial requirement is delivery of an adequate level of "lethality" to the product. The use of F_0 is recognised with an F_0 of 8 being the usually acceptable minimum. It is emphasised that this requires a low pre-sterilization bioburden and the absence of heat resistant spores.

Calculation of F_0 values

A3.9 Reliable F_0 value calculations are simply achieved with modern microprocessor based control and monitoring systems. However F_0 values can be calculated manually, and many of the available computer programs employ essentially similar methods:

a. *Graphical method.* In the graphical method *F* reference paper is used on which the lethal rate per minute, at particular temperature, is represented by length on the vertical axis. The horizontal axis has a corresponding arithmetic scale for time such that the area of a rectangle delineated by the ordinate 121.1°C and a length corresponding to one minute on the abscissa is equal, by definition to an F_0 of one. The cumulative area under the curve as the cycle progresses represents the cumulative lethality of the process (see Figure A8). In practice the temperature profile is plotted and the area under the curve determined using a planimeter. The area measured is then converted to an F_0 value using the scale of the *F* reference paper.

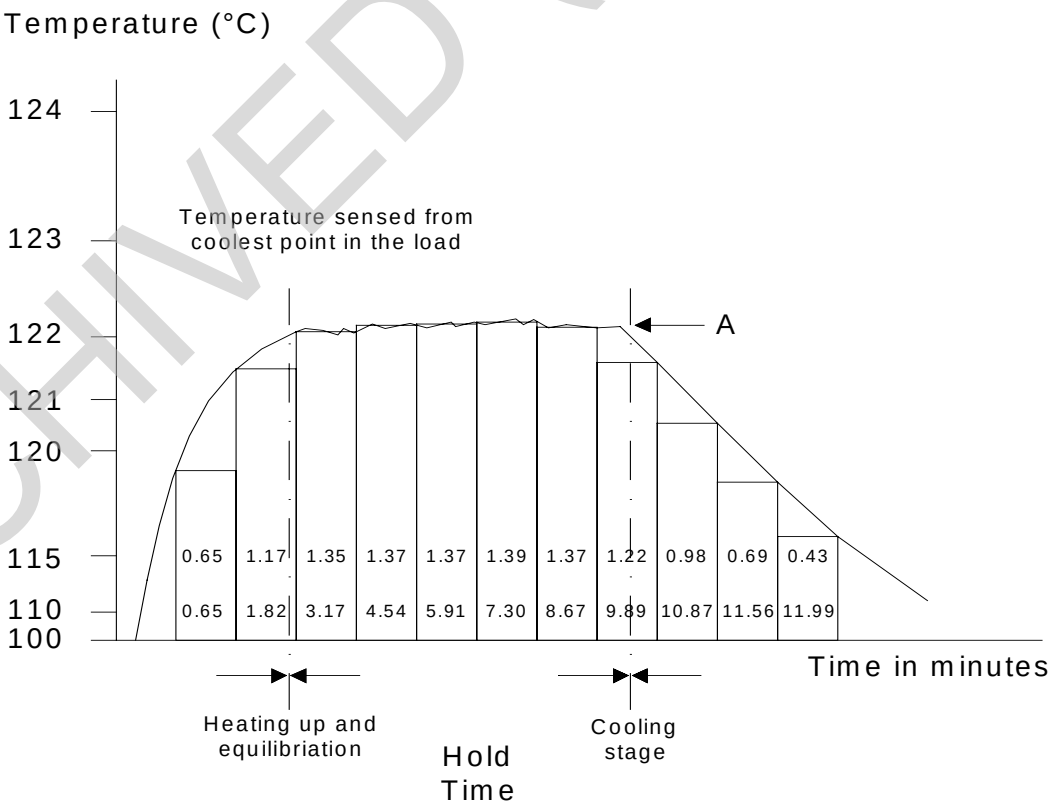
b. *Summation method*. In the summation method the lethal rate at each specific temperature is calculated or read from a table (see Table A1) and multiplied by the time for which that temperature persisted. The values obtained for each temperature are summed to give the overall F_0 value for the cycle.

A3.10 The accuracy of the integration is affected by a number of factors.

These include:

- the choice of time interval between successive temperature measurements. BS 3970 Part 2 specifies a maximum interval of two seconds;
- whether the minimum, maximum or average temperature during the chosen time interval is used. (Since the method is an approximation based on summing discrete data to represent continuous data there will always be some error, which may be positive or negative; each may be correct for different purposes);
- the location of the sensor(s) from which the temperature is read and the adequacy of the validation of sensor location;
- should be used only over the temperature range for which *Z* has been determined. The *Z* value for any micro-organism does not remain constant over all possible temperatures. Therefore any particular lower temperature limits for the integration need not be set since, for a Z value of 10, F_0values below 105°C make so little contribution. For example, 40 minutes exposure at 105°C is equivalent to one minute at 121°C.

Figure A8: Graphical determination of F_0 values



The ordinate scale (temperature) of *F*-reference paper is proportional to the lethal rate so that the area beneath the curve is a measure of the *F* value. The cumulative values during the cooling stage are not used for sterilizer control but may be used in monitoring to provide an accurate assessment of the overall lethality delivered by the sterilization cycle. Within each box the figures in italics indicate the F_0 value calculated for that time-temperature rectangle. The lower figures indicate the cumulative F_0 value through the cycle. The F_0 controller, set to provide an F_0 value of 9, initiates the cooling stage at point A. The total monitored F_0 value of the cycle is 11.99.

A4. Applications of the F_0 concept

General

A4.1 Part 3 of this SHTM states that if a fluid sterilizer is fitted with an F_0 integrating system, then the recorder should be capable of computing and printing values of F_0 for each channel with integration times no greater than 2 s. This is also a requirement of BS 3970: Part 2.

Control of sterile cooling fluid (in a steam sterilizer for fluids in sealed containers)

A4.2 It is a requirement that if the coolant is derived from a water or steam service and is intended to come into contact with the load containers, the operating cycle must expose the coolant to sufficient heat to ensure that it is free of microbial contamination by the end of the holding time. This is checked by calculating an F_0 value for the heat treatment received by the coolant. If the test recorder is not capable of calculating F_0 both BS 3970 and Part 3 of this SHTM recommend the following procedure:

a. from the measured temperatures, identify the point during the heat-up time at which the coolant temperature first reaches 108°C. Note the temperature (T°C) at subsequent one minute intervals until the end of the holding time;

b. for each measurement, calculate the incremental F_0 (ΔF_0) from the following equation:

$$\Delta F_0 = \log_{10}\left[\frac{T - 121}{10}\right] \text{ minutes}$$

where T is the lowest temperature of the coolant water for each one minute time interval

c. the F_0 value is the sum of all ΔF_0.

The test should be considered satisfactory if the F_0 for the coolant is not less than 8 minutes.

F_0 controlled sterilizers – Control of operating cycles in steam sterilizers for fluids in sealed containers

A4.3 The operating cycle for steam sterilizers used to process aqueous fluids in sealed containers may be divided into several stages.

1. heat up (and, where necessary, air removal) – the chamber atmosphere attains the required temperature;
2. equilibration time – all parts of the load attain or exceed the minimum temperature of the sterilization temperature band;
3. holding time – all parts of the load are maintained at a temperature within the sterilization temperature band;
4. cooling stage – the load is cooled to a temperature at which it will be safe to handle.

A4.4 Stages 2 and 3 may be controlled by one of the following:

a. adjustable timers of an automatic controller in conjunction with temperature sensors within the active chamber discharge and within containers of the load;
b. a simulator control system;
c. an F_0 system.

A4.5 Provision for adjustment of the equilibration time (stage 2) is necessary and may be achieved by one of the following:

a. an operator adjustable timer on the instrument panel;
b. a simulator control system;
c. an F_0 integrating system.

A4.6 When an F_0 control system is fitted, the control function should be limited to the initiation of the cooling stage (stage 4) once a selected F_0 value has been attained.

A4.7 In addition to the minimum requirement of two temperature sensors (see 13.1.4 of BS 3970 Part 1) two further temperature sensors shall be provided for use in two load containers.

A4.8 The control system shall be designed to integrate from the temperatures sensed within containers of the load at selected locations at time intervals not exceeding 2 seconds.

A4.9 The range of F_0 values selectable shall include 1 to 30.

A4.10 When tested in accordance with Test method 1, the Individual values of F_0 determined using the reference instrument shall be within the ranges stated in Table A2 for each of the F_0 values indicated by the sterilizer under test.

Table A2: Permitted Ranges For F_0 Values

F_0 value indicated by sterilizer under test	Permitted range for F_0 values determination by the reference instrument*
1	1 to 1.05
15	15 to 15.7
30	30 to 31.5

* The reference instrument is described in Test method 2

Monitoring operating cycles in steam sterilizers for fluids in sealed containers

A4.11 For aqueous products in sealed containers temperatures are measured (with thermocouples or RTDs) throughout the heating and cooling stages as well as during the sterilization hold period. The slowest container to heat and the fastest container to cool may be used to determine the minimum lethality received by the load. these locations are often found in different locations.

A4.12 Determination of the maximum temperatures in the load may also be necessary for thermolabile products where deterioration may be a problem.

A4.13 It is essential that during commissioning and validation it is established that the position of containers which need to be monitored remains consistent from cycle to cycle. A sterilizer where the slowest part of the load to reach temperature is found in different parts of the load on successive cycles is not suitable for control or monitoring by F_0 values and is in urgent need of skilled attention. For air-ballasted sterilizers this may involve additional requirements on monitoring the circulation of the chamber atmosphere to ensure that the location of the cool point remains constant.

A4.14 Calculation of the F_0 value delivered by a process may be estimated from the lowest temperature-time curve registered from the containers in the load. The process is satisfactory if the registered F_0 value is within the minimum and maximum limits established during validation.

Validation of operating cycles in steam sterilizers for fluids in sealed containers

A4.15 The use of F_0 control or monitoring systems places additional requirements on the validation process.

A4.16 As described in Part 3 of this SHTM, paragraph 8.4 ’Sterilizer function using a full load’ ’... the temperature of all sites monitored within the load ..... shall be within 1°C of each other throughout stage 3'. This requirement applies regardless of whether an F_0 system is used.

Container cool point

A4.17 Container mapping is necessary to determine the container cool point. Container mapping studies should be conducted prior to conducting loaded chamber heat penetration studies in order to determine the position within the liquid-filled container which is slowest to attain temperature.

A4.18 Small volume containers and those of cylindrical form where the length:diameter ratio is large are the least likely to demonstrate a detectable cold spot.

The number of thermocouples within the container should be sufficient to monitor the upper, middle and lower layers of the central region of the container. Using an excessive number of temperature probes may introduce significant errors in the determination.

A4.19 The profile point requiring the longest exposure time to equilibrate with the chamber temperature should then be used in subsequent F_0 studies and monitoring (but see later for degradation/product stability considerations).

A4.20 Suitable container entry systems for the insertion of temperature probes into sealed containers are described in part 3 of this SHTM (Figure 3).

A4.21 Independent measuring equipment should be to the standard described in part 3 of this SHTM, Chapter 6.

A4.22 The test should be carried out as described in part 3 of this SHTM for a thermometric test for a full load (see paragraph 14.10) except that the load should be containers of the type and number to be used in practice and filled with the product to be sterilized or a suitable substitute with similar thermal characteristics, (see paragraph A4.31 below).

Load cool point

A4.23 It is necessary to determine the coolest point within a specified load type and configuration of load. Cool points arise because of varied rate of heat transfer throughout the load and studies are needed to ensure that the cool points are identified so that they may be exposed to sufficient heat lethality.

A4.24 The study is carried out in the same manner as the performance qualification described in part 3 of this SHTM (see paragraphs 8.13 to 8.28 performance qualification).

A4.25 Similar studies may be used to identify those containers which attain temperature maxima or most prolonged exposure to the equilibrium temperature for product degradation and/or stability studies.

A4.26 The F_0 value for the process may then be determined by integrating the lethal rates throughout the heating process using one of the methods previously described.

Microbial challenge studies

(See also part 3 of this SHTM paragraphs 8.29 to 8.36)

A4.27 Biological challenges may be used during validation studies in order to demonstrate the process lethality provided by the sterilization cycle. Calibrated biological indicators used for this purpose act as bioburden models and can be used in obtaining data to calculate F_0 values delivered by the cycle or to supplement physical temperature measurement, for example from thermocouples.

A4.28 The number of spores to be used in the BI can be calculated from the following formula

$$D_{prod} (\log N_{prod} + 6) = D_{bi} (\log N_{bi} + 1)$$

Where D_{prod} = the resistance of the most resistant organism in the product bioburden;

N_{prod} = the number of organisms in the product to be sterilized;

D_{bi} = the resistance of the BI organism;

N_{bi} = the number of organisms on the BI.

A4.29 Designated liquid-filled containers are inoculated with the indicator organism by injecting an aliquot of a calibrated spore suspension into the suspending menstruum to provide the calculated concentration of spores. The containers chosen should be those previously established by temperature measurement as having the lowest delivered lethality.

A4.30 The suspending menstruum should be the product to be sterilized unless this contains preservatives, antimicrobials or other substances which inhibit the growth of the indicator micro-organisms.

A4.31 If it is necessary to use a product substitute it should be selected to have similar physical characteristics to the product this should include heat capacity (specific heat), density, viscosity, thermal conductivity.

A4.32 Great care needed when using inoculated product to minimise the possibility of contaminating the production environment.

A4.33 Microbial challenge studies should be conducted concurrently with heat penetration studies.

Product degradation and stability versus cycle lethality

A4.34 When heat-sensitive thermolabile products are to be sterilized it is important that adequate assurance of sterility is not obtained at the expense of product degradation or stability.

A4.35 For sterilization the temperature dependence of the process is described by the Z value, that is the change in temperature required to give a tenfold change in the rate of microbial kill. Increasing or decreasing the temperature of the process requires a corresponding decrease or increase in exposure time to maintain the same cycle lethality or F_0 value.

A4.36 For any given temperature, microbial death and chemical degradation take place at different rates. The relationship between time and temperature which exists for microbial lethality cannot be extrapolated to the product degradation reaction.

A4.37 If the degradation reaction is not altered significantly by the change in temperature the extent of degradation will increase as process (exposure) time is extended. Conversely, if the degradation reaction is highly temperature dependent (high activation energy) a decrease in temperature may more than compensate for the increase in time, resulting in less degradation.

A4.38 The key variable is the activation energy, E_A . If the activation energy for the chemical degradation reaction is lower than that of the microbial death curve, that is it is less temperature dependent, then it can be assumed that a decrease in sterilization temperature will result in greater product degradation.

A4.39 Furthermore it cannot be assumed that sterilization cycles of equivalent lethality, but which differ with regard to time and temperature, will yield product of equal quality.

A4.40 The assumption that degradation reactions follow first-order reaction kinetics is probably a good approximation in most cases where a single active drug product is contained in the solution.

A4.41 Experience has shown that a decrease in sterilization temperature can have a marked deleterious effect on product and its long term stability.

A4.42 Sterilization of glucose solutions in plastic containers may require a sterilization temperature in the range 115-118°C in order to protect the thermolabile container. The increased time required for sterilization compared with a traditional cycle at 121°C used for similar solutions in glass bottles results in a noticeable increase in caramelization.

A4.43 The activation energy of the lethal reaction for bacterial spores with a *Z* value of 10°C is high (typically around 60 kcal/mole) compared to most first-order liquid-phase decompositions. Thus products that degrade with heat are more affected by an increase in time than an increase in temperature. For example, expressed as a *Z* value the temperature effect of the degradation of glucose would have a *Z* value of about 33°C.

A4.44 The use of *F* values based on the *Z* value of the most resistant contaminating organism found during bioburden studies rather than an assumed *Z* value of 10°C may be necessary for particularly thermolabile products. Great care is needed in the application of this technique because

of the inherent variability of microbial contamination and the rigorous process control and monitoring needed to minimise this.

Product stability

A4.45 Product stability may also be related to degradation during sterilization. Chemical reaction kinetic studies on many products indicate that product stability over the desired shelf life can be extrapolated from the extent of degradation measured just after sterilization. In some cases a degradation product formed during sterilization triggers subsequent deterioration and the specific factors affecting the formation of the degradation product would need to be investigated.

A4.46 Both microbial lethality and degradation are cumulative with respect to time and temperature, so variations in the heating and cooling phases of the cycle will affect the extent of degradation, and thus product stability, as well as lethality.

A4.47 Degradation and stability studies should consider the entire cycle and not just the dwell time. These effects are more pronounced for products where the degradation reaction has a lower activation energy.

A4.48 F_0 values are generally calculated from the coolest part of the load. For degradation and stability purposes the hottest part of the load is of more consequence. The entire range of temperature and time experienced throughout the load must be recorded in order to substantiate degradation and stability claims.

Cycle development studies

A4.49 Determination of F_0 values is often of value in the development of appropriate operating cycles for steam sterilization of both fluids in sealed containers and wrapped goods and porous loads. However, since temperature measurement alone cannot reliably detect failure to obtain direct contact with dry saturated steam, it is not practicable to use F_0 values for monitoring or controlling porous load cycles.

The use of F_0 values for porous load cycles should be limited to determining suitable sublethal cycles for biological challenge studies.

A5. Test methods

Test for F_0 control compliance

Apparatus

A5.1 Glass bottle, of nominal capacity 1 litre, complying with DIN 58363.

A5.2 Independent F_0 reference instrument, as described in section F.

Procedure

A5.3 Install the reference instrument.

A5.4 Place 1 litre of cold water in the bottle. Insert the two temperature sensors of the F_0 control system and the sensor of the reference instrument so that the sensing points of all three are at about 85% of the bottle depth and over the approximate centre of the bottom of the bottle. Seal the bottle.

A5.5 Select the required F_0 value on the control panel and perform a cycle in which automatic control is terminated manually immediately at the beginning of stage 4. Note the value of F_0 shown by the reference instrument.

A5.6 Repeat the procedure described in paragraph A5.5 twice.

A5.7 This test procedure shall be carried out for F_0 values of 1, 15 and 30.

A5.8 Calculate the mean of the three replicate values for each setting of F_0 control and check for compliance with the values given in Table A2.

Test for performance of reference instrument

Apparatus

A5.9 Temperature regulated heat source capable of being controlled at a given temperature within 0.10°C in the range 115°C to 126°C.

A5.10 Thermometer traceable to national standards to include the range 100°C to 130°C complying with BS 593 and graduated at intervals of 0.1°C.

A5.11 Temperature logging device computing F_0 values of the sensor(s) with integration at least every 2 s and means of print out, together with suitable temperature sensor(s).

A5.12 Stopwatch.

Procedure

A5.13 Install the sensor(s) into the temperature regulated heat source.

A5.14 Adjust the heat source so that it maintains a temperature of 121±0.1°C.

A5.15 Allow the equipment to integrate F_0 for 15 minutes timed with the stopwatch. Note the indicated F_0 value.

A5.16 Repeat with the temperature source maintained at 115±0.1°C for 30 min.

A5.17 Repeat with the temperature source maintained at 126±0.1°C for 10 min.

A5.18 The replicate F_0 values obtained at 121°C shall lie within the range 14.66 to 15.34.

A5.19 The replicate F_0 values obtained at 115°C shall lie within the range 7.36 to 7.71.

A5.20 The replicate F_0 values obtained at 126°C shall lie within the range 30.90 to 33.36.

Glossary

D value The *D* value (or Decimal Reduction Value) is a measure of the resistance of a micro-organism to a particular type of sterilization process. It is the value of the appropriate parameter of the process (duration or absorbed dose) required to reduce the number of viable micro-organisms to 10% of the original number.

In connection with sterilization by heating in an autoclave the D value is expressed by the time minutes at a defined temperature (the temperature is often shown as a subscript, for example D_{121}).

Z value In connection with sterilization by heating in an autoclave the Z value relates the heat resistance of a micro-organism to changes in temperature. The Z value is the change in temperature required to alter the D value by a factor of 10.

F_0 A quantity, measured in minutes, used to determine the efficacy of an operating cycle and equivalent to a continuous period at a temperature of 121.1°C for an organism with a Z value of 10°C.

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Section B

Methods for determining the fatigue life of rectangular pressure vessels

B. Methods for determining the fatigue life of rectangular pressure vessels

This section is not included. Please refer to the printed version of BS 3970.

Section C

Packaging for terminally sterilized products

Contents

C1. Introduction

C1.1 This section discusses the factors which should be considered in the selection and use of packaging for terminally sterilized products, that is, those materials which are sterilized in their packaging.

Packaging for medical equipment which has been cleaned, decontaminated/disinfected and serviced ready for return to use is not included in this guidance.

C1.2 It does not consider those products which are sterilized and then aseptically packed in sterilized packaging materials nor does it cover packaging of terminally sterilized components to be used in aseptic manufacturing.

Sterilization processes

C1.3 Because the product is sterilized in its packaging it is necessary that the packaging maternal is compatible with the sterilization process to be used.

C1.4 The sterilization processes included are those which are generally available for use either directly or through a sub-contractor. It does not include requirements for new processes which are currently under development or at an early stage of their introduction for practical use. This would include, for example, those systems employing gaseous or plasma phase peracetic acid and/or hydrogen peroxide.

C1.5 Sterilzation processes included are:

a. Steam – for clinical use (see SHTM 2010 Part 1, paragraph 2.1 (a)):
   (i) for wrapped goods and porous loads;
   (ii) for aqueous fluids
      - in rigid containers;
      - in flexible containers;
   (iii) for unwrapped instruments and utensils
      - externally supplied steam;
      - internally generated steam;
b. Steam – for laboratory use (see SHTM 2010 Part 1, paragraph 2.1 (b)):
c. Low-temperature steam and formaldehyde. Note. The packaging materials, systems and procedures described are also suitable for use with disinfection processes intended for use with wrapped goods, for example Low Temperature Steam Disinfectors (LTS);
d. Ethylene oxide;

e. Dry heat (hot air);

f. Ionising irradiation (gamma and beta).

Product applications

C1.6 The sterile products for which packaging is considered include:

- medical devices and surgical instruments:
  - primarily those products, including re-usable instruments, utensils and textiles, which are processed by Sterile Service Departments, including units directly serving operating theatres (although the same principles apply to other manufacturing systems which have a wide range of product specifications produced singly or in small numbers. Only passing reference is made to high speed automated packaging systems.);
  - re-usable instruments processed in clinics and general practices (dental and medical);
- pharmaceutical manufacturing of sterile products;
- laboratory product manufacturing, for example culture media for microbiology;
- discard (or make-safe) prior to disposal of potentially infective material.

C1.7 Consideration is given to materials and systems for both single-use and re-usable packaging.

C1.8 Single-use packaging includes, for example, ampoules, single-trip bottles, paper bags, paper/plastic pouches & reels, paper wraps, vacuum formed trays, etc.

C1.9 Re-usable packaging includes, for example, multiple-trip bottles, procedure trays, sterilization containers, textile wraps, etc.

C1.10 This guidance section also makes reference to labelling, storage and distribution giving both guidance and particular requirements necessary to ensure compliance with extant regulations.

Responsibility

C1.11 Part 1 of SHTM 2010 (paragraph 1.15 (h)) Identifies the procedures for production, quality control and safety as a major responsibility of management.

C1.12 The provisions of this section should be reviewed by those responsible for the management of sterile production and adapted to local circumstances (for example taking into consideration the nature of the product, the volume of production, the sterilization process(es) available etc.).

C1.13 It should be used as the basis for the development of written policies, specifications and procedures to be used in the control of sterile production.

General performance requirements

C1.14 The purposes for which packaging is used are:

- to contain the product;
- to permit sterilization of the packaged product;
- to protect the product from deterioration and damage;
- to maintain the sterility of the product through distribution and storage to the point of use;
- to prevent contamination of the product.

C1.15 In addition the packaging must:

- permit identification of the number and type of product contained, the lot number, the manufacturer and the expiry date (by labelling);
- include specification of storage conditions which the packaging is designed to withstand;
- provide any necessary instructions for the correct use of the product (by labelling and/or instruction sheets);
- present the product in a manner which allows it to be removed aseptically immediately before use.

Packaging operations

C1.16 The procedures and controls implemented for packaging operations must be designed to ensure that:

- each product produced is in the correct type of pack;
- each pack is correctly and effectively sealed;
- each pack is correctly labelled with all the necessary information.

Quality control

C1.17 The nature of packaging for terminally sterilized products is such that:

- it is not possible to test the packaging on finished product in a manner which permits its subsequent distribution for use;
- it is not possible to test any one sample for all necessary characteristics;
- it is not possible to test each pack immediately before use to ensure that the packaging has performed correctly throughout sterilization, distribution and storage.

C1.18 Adequate control of the quality of packaging can only be obtained through a comprehensive programme including:

- design, and design verification;
- specification of packaging procedures;
- validation of packaging procedures;
- control of purchased material;
- control and monitoring of the packaging process;
- training for all who produce, handle or use sterile packs.

C1.19 Labelling is an essential part of packaging and procedures are required to ensure that particular care is taken to avoid labelling errors.

C1.20 The importance of proper control over all aspects of the packaging process cannot be over-emphasised. When products such as medical devices or medicinal products are presented wrongly labelled, contaminated, or damaged their use can cause serious adverse effect and may, in extreme cases, be lethal.

C2. Regulatory requirements and standards

C2.1 So far as requirements for packaging, including labelling, are concerned, the chief areas of legislation with which managers should be familiar are those concerned with safety, consumer protection, medicinal products, medical devices, active implantable medical devices and in vitro diagnostics.

The legislation relevant to sterilizers is also discussed in SHTM 2010 Part 1, Chapter 3, to which reference should be made.

Safety

C2.2 Manufacturers have two specific obligations under the Health and Safety at Work etc Act 1974:

1. to take all reasonably practicable steps to ensure that their products have been designed and manufactured so as to be safe when used for the intended purpose;
2. to ensure that persons who use their product in further manufacturing and retailing operations have adequate information and advice about how the products should be used to ensure safety.

C2.3 There is also a more general requirement under common law to protect all persons involved with the use of the product.

Medicinal products

C2.4 Where a packaging material or system is used to contain a medicinal product the licensing provisions of the Medicines Act 1968 apply.

Further information may be found in ‘Guidance to the NHS on the licensing requirements of the Medicines Act 1968’ published by the Medicines Control Agency.

C2.5 The Medicines (Standard Provisions of Licences and Certificates) Amendment Regulations 1992 (Sl 1992/2846) give statutory force to the European Commission document ‘The rules governing medicinal products in the European Community Volume IV Guide to Good Manufacturing Practice for medicinal products’.

Guide to Good Manufacturing Practice for medicinal products

C2.6 The principles and detailed guidelines of good manufacturing practice deal with a number of aspects of packaging including:

- Documentation, which should include:
  - a formal, written specification for packaging materials;
  - formally authorised packaging instructions for each product, pack size and type;
  - a record kept for each batch or part batch processed.
- Purchase, handling and control should be treated in the same manner as starting materials with particular attention paid to printed material;
- Packaging operations should be designed to minimise the risk of mix-ups by the inclusion of a line clearance procedure and special care should be exercised to avoid mislabelling.

The packaging should be verified as being of the correct type, clean and in the correct quantity and there should be suitable on-line control and monitoring to verify the adequacy of the packaging operation.

Consumer protection

C2.7 Part 1 of the Consumer Protection Act 1987 implements Directive 85/374/EEC (the Product Liability Directive) and provides for compensation to be paid to persons suffering injury from a defective product. The implications of this legislation are discussed in SHTM 2010 Part 1 (paragraphs 3.26 to 3.28 inclusive).

Active Implantable Medical Device Regulations 1992

C2.8 The Active Implantable Medical Devices Regulations 1992 (Sl/1992/3146) implements Council Directive 90/385/EEC. Schedule 2, paragraph 7 of these regulations requires active implantable medical devices to be designed, manufactured and packed in a non-reusable packaging according to procedures which are sufficient to procedures which are sufficient to ensure that:

a. the device is sterile when placed on the market;

b. if handled in accordance with conditions as to storage laid down by the manufacturer, the device remains sterile until the packaging is removed and the device is implanted.

Medical Devices Regulations

C2.9 The Medical Devices Regulations 1994 (SI/1994/3017) implements Council Directive 93/42/EEC of 14 June 1993 concerning Medical Devices and came into effect on 1 January 1995.

C2.10 Regulation 11 concerns the procedure for systems and procedure packs and requires, inter alia, that any person who puts devices bearing the CE marking together, within their intended purpose and within the limits of use specified by their manufacturers, in order to place them on the market as a system or procedure pack, shall draw up a declaration by which he states that he has packaged the system or procedure pack and supplied relevant information to users incorporating relevant instructions from the manufacturers, and that the whole activity is subjected to appropriate methods of internal control and inspection.

C2.11 The Essential Requirements described in Annex 1 (of the Directive) include a number of specific requirements for packaging and labelling which are summarised below.

General requirements

C2.12 The devices must be designed, manufactured and packaged in such a way that they are suitable for the functions specified by the manufacturer.

C2.13 The devices must be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected during transport and storage taking account of the instructions and information supplied by the manufacturer.

Requirements regarding design and construction

C2.14 The devices be designed, manufactured and packed in such a way as to minimise the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to the patients taking into account the intended purpose of the product.

C2.15 The devices and manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and third parties.

C2.16 Devices delivered in a sterile state must be designed, manufactured and packed in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market and remain sterile under the storage and transport conditions laid down, until the protective packaging is damaged or opened.

C2.17 Packaging systems for non-sterile devices must keep the product without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilized prior to use, minimise the risk of microbial contamination; the packaging system must be suitable taking account of the method of sterilization specified by the manufacturer.

C2.18 The packaging and/or label of the device must distinguish between identical or similar products sold in both sterile and non-sterile condition.

C2.19 Each device must be accompanied by the information needed to use it safely and to identify the manufacturer, taking into account the training and knowledge of the users.

C2.20 This information comprises the data on the label and the data in the instructions for use.

C2.21 As far as practicable and appropriate, the information needed to use the device safely must be set out on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging.

C2.22 If individual packaging of each unit is not practicable the information must be set out in the leaflet supplied with one or more devices.

C2.23 Instructions for use must be included in the packaging for every device. By way of exception, no such instructions for use are needed for devices classified in Class I or IIa if they can be used safely without any such instructions. The majority of, but not all, products produced in hospital based sterilization units would fall into this category, for example re-usable surgical instruments which are in Class I. Exceptions include implants, and may include devices intended for use on skin wounds that have breached the dermis. In case of doubt reference should be made to the classification criteria given in Annex IX of the directive or advice sought from the competent authority (Medical Devices Agency, DoH).

C2.24 Where appropriate this information should take the form of symbols. Any symbol or identification colour used must conform to the harmonised standards. In areas for which no standards exist, the symbols and colours must be described in the documentation supplied with the device.

C2.25 The label must bear the following particulars:

a. the name and trade address of the manufacturer;

b. the details strictly necessary for the user to identify the device and the contents of the packaging;

c. where appropriate, the word STERILE;

d. where appropriate, the batch code, preceded by the word LOT, or the serial number;

e. where appropriate, an indication of the date by which the device should be used, in safety, expressed as the year and month;

f. where appropriate, an indication that the device is for single use;

g. if the device is custom made, the words “custom made device”;

h. if the device is intended for clinical investigations, the words "exclusively for clinical investigations";

i. any special storage and/or handling conditions;

j. any special operating instructions;

k. any warnings and/or precautions to take;

l. year of manufacture for active devices other than those covered by e. This indication may be included in the batch or serial number;

m. where applicable, method of sterilization.

C2.26 If the intended purpose of the device is not obvious to the user the manufacturer must clearly state it on the label and in the instructions for use.

C2.27 Wherever reasonable and practicable, the devices and detachable components must be identified, where appropriate in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components.

C2.28 Where appropriate the instructions for use must contain the following particulars:

1. information to avoid certain risks in connection with implantation of the device;
2. the necessary instructions in the event of damage to the sterile packaging and where appropriate details of appropriate methods of re-sterilization;
3. if the device is reusable, information on the appropriate processes to allow re-use, including cleaning, disinfection, packaging and, where appropriate, the method of sterilization of the device to be re-sterilized, and any restriction on the number of re-uses.

C2.29 Where devices are supplied with the intention that they be sterilized before use, the instructions for cleaning and sterilization must be such that if correctly followed the device will still comply with the general requirements specified in Section 1, Annex 1 of the directive.

C2.30 The instructions for use must also include details allowing the medical staff to brief the patient on any contra-indications and any precautions to be taken.

Glass containers EEC Directive 75/107

C2.31 Capacity tolerances for bottles specified as measuring containers were defined in the Directive and are summarised in Table C1.

Two methods of capacity verification were specified, the Standard deviation method and the Mean range method.

Table C1: Capacity tolerance for bottles as measuring containers

Nominal capacity C (ml)	Capacity tolerances as %	
	of C	in ml
50 – 100	–	±3
100 – 200	±3	–
200 – 300	–	±6
300 – 500	±2	–
500 – 1000	–	±10
1000 – 5000	±1	–

British and European standards

C2.32 The rapid development in European Standards, which are required to be adopted as national standards by all European members of the European Committee for Standardisation (CEN), is largely due to the role that such standards have in demonstrating compliance with legislation implementing European Directives.

CEN is recognised by the European Union as a competent body for the adoption of harmonised standards.

C2.33 For the purpose of the European Directives on Medical Devices and Active Implantable Medical Devices a harmonised standard is a technical specification (European standard or harmonisation, document) adopted, on a mandate from the European Commission, by CEN.

C2.34 There is a presumption of compliance to the essential requirements of the Directive for devices which are in conformity with the relevant harmonised standards the references of which have been published in the Official Journal of the European Communities.

C2.35 A number of standards are in preparation which are relevant to packaging and labelling of terminally sterilized products.

The following list is not exhaustive. The standards discussed are in various stages of preparation, those marked * are finalised and published. All EN standards are available in the UK as British Standards; there is now a dual numbering system so that EN *** will be numbered as BS EN ***.

C2.36 EN 1041 *Terminology symbols and information provided with medical devices - Information supplied by the manufacturer with medical devices*

This standard specifies the information to be supplied by the manufacturer of medical devices necessary to comply with the requirements of the Directive.

C2.37 **EN 980** *Terminology symbols and information provided with medical devices - Graphical symbols for the labelling of medical devices*

This standard defines a number of symbols to be used in labelling medical devices. The use of these symbols will both facilitate provision of all the essential information on small packs and minimise the need for multi-lingual labelling.

C2.38 **EN 868 series** *Packaging materials for sterilization of wrapped goods*

This standard is presented in a series of separate parts. The first part specifies the general requirements for packaging materials to be used for medical devices which are to be terminally sterilized and provides requirements, guidance and test methods for the validation of packaging materials and systems.

The subsequent parts of the standard specify requirements for a variety of packaging materials and systems. Conformity with the specified requirements in these parts of the standard may be used as one means of demonstrating compliance with some, or all, of the requirements of Part 1.

C2.39 **EN 867 series** *Non-biological systems for testing sterilizers*

This series of standards specifies the requirements for chemical indicators used in testing sterilizers. Part 2 of the standard specifically addresses the performance requirements for process indicators, whether used independently of, or printed on, labels or packaging materials. Detailed specifications are given for performance criteria relevant to all the sterilization processes considered in this Section (see paragraph C1.5).

C2.40 **EN 724** *Guidance on the application of EN 29001 and EN 46001 and of EN 29002 and EN 46002 for non-active medical devices*

This standard provides guidance on suitable methods and procedures, including aspects of packaging, for the manufacture of medical devices in conformity with the requirements of the Quality System standards which may be used to demonstrate compliance with the requirements of the Directive.

C2.41 **EN 550*** *Sterilization of medical devices - Validation and routine control of ethylene oxide sterilization*

This standard specifies requirements for the development, validation, process control and monitoring of the sterilization of medical devices using ethylene oxide and gives guidance on means by which these requirements may be met. The importance of packaging in the correct functioning of an ethylene oxide sterilization process is recognised.

C2.42 **EN 552*** *Sterilization of medical devices - Validation and routine control of sterilization by irradiation*

This standard specifies requirements for the development, validation, process control and monitoring of the sterilization of medical devices using ionising radiation and gives guidance on means by which these requirements may be met. The importance of specifying and controlling packaging from validation through to routine batch control is emphasised.

C2.43 **EN 554*** *Sterilization of medical devices - Validation and routine control of sterilization by moist heat*

This standard specifies requirements for the development, validation, process control and monitoring of the sterilization of medical devices using moist heat.

The methods used are based on monitoring physical factors and control of the packaging is an essential part of the system.

C2.44 **EN 1174** series *Sterilization of medical devices - estimation of the population of micro-organisms on product*

This standard describes methods for determining the extent of microbial contamination on products, including packaging, prior to sterilization.

C3. Design considerations

C3.1 The manufacturer of the sterile product is responsible for adopting a design for the pack which is suitable for its intended purpose.

C3.2 However, in many cases the design of the packaging material and/or system may be controlled by the manufacturer of the packaging material and/or packaging system and sold as suitable for a particular range of applications.

C3.3 The choice of such a pre-designed, commercially available packaging system does not absolve the sterile product manufacturer from the responsibility for ensuring that:

- the design of the packaging system, including the selection of materials, is suitable in all respects for the intended application (see Chapter C6)
- the packaging system as received from the supplier is in conformity with the specification against which the choice was made (see Chapter C5)
- the production facilities, including the skills of production personnel, are compatible with the packaging system chosen and have the demonstrated capability to fill, seal and sterilize the packaging in accordance with the instructions provided by the manufacturer of the packaging system, (see Chapters C7 - C9).

C3.4 The packaging is required to fulfil a number of functions. These may be summarised as: “to minimise the safety hazard to the manufacturer, user or patient arising from interaction of the product with its environment under the conditions of sterilization, transport, storage and use as specified by the producer of the packaging system and/or sterile product”.

C3.5 The design should include consideration of at least the following:

- the compatibility of the packaging with the sterilization process;
- the compatibility of the packaging with the labelling system;
- the compatibility of the packaging with the users’ requirements at the point of use, for example aseptic opening;
- the sensitivity of the pack contents to particular risks, for example irradiation, moisture, mechanical shock, static discharge.
- the compatibility of the packaging with the contents, for example the medical device or medicinal substance, in order that the packaging has no adverse effect on the medical device or vice versa;
- the protection provided by the packaging against adverse environmental influences which may reasonably be anticipated, for example mechanical shock, vibration, chemical or microbial contamination;

C3.6 The emphasis to be given to each of these considerations will be different for each of the various sterile products manufactured but, compatibility with the sterilization process and the subsequent protection against microbial contamination are paramount in providing the user with a sterile product.

C3.7 In many cases historical data may be used to provide satisfactory evidence that the packaging is suitable for its intended purpose where packaging to the same specification has previously been used satisfactorily for a particular product, or one that is similar in all essential respects.

C3.8 The design documentation should include details of the product to be packaged, the sterilization process to be used, the storage and transport conditions as well as the specification of the packaging materials and processes to be used.

Compatibility with the sterilization process

C3.9 There are two important aspects to sterilization compatibility:

a. the ability of the packaging material to permit the attainment of the required conditions for sterilization in the process with which it is intended to be used;

b. the ability of the packaging material to withstand the sterilization process without deterioration which adversely affects its protective performance.

C3.10 Both attributes should be demonstrated.

Moist-heat/steam sterilization processes

C3.11 For effective sterilization by moist heat all parts of the load should be in contact with water or saturated steam at the required temperature for the required time.

Sterilizers for wrapped goods and porous loads

C3.12 Items to be sterilized, other than aqueous products in sealed containers, should be packaged in a pack which allows removal of air and penetration of steam but which prevents recontamination after sterilization.

C3.13 This is normally achieved by the use of materials which are permeable to air and steam but have an effective maximum pore size which is small enough to exclude microbial contamination under the specified storage and transport conditions.

C3.14 This includes wrapping in porous materials, the use of rigid containers which are fitted with filters or valves, or a combination of these methods.

C3.15 Effective sterilization requires complete permeation of the porous materials with the moisture and heat of the steam. This may occur rapidly or slowly and depends, inter alia, on the size and density of the pack, the method of air removal, the nature of the porous material etc.

C3.16 With packaged solid, hollow or fibrous products air may become trapped, randomly, in the sterilizer chamber and load. The microbial lethality of elevated temperatures under dry and moist conditions are vastly different. The presence of air can cause an unacceptable impairment of the sterilization process.

C3.17 Unpredictable air retention is of particular concern with porous wrapping materials. Hence for effective sterilization of wrapped goods and porous loads it is important to employ a sterilization process which incorporates forced air removal prior to the sterilization stage.

C3.18 Preliminary tests on the product and its packaging in order to determine the levels and rates of change of pressure, temperature and vacuum which start to cause unacceptable changes in the performance qualities of the medical device and/or its packaging may be necessary.

C3.19 Performance qualification should be performed on the introduction of new or modified packaging unless equivalence either to a validated reference load or to previously validated packaging has been demonstrated.

C3.20 Materials used for packaging should be compatible with the sterilization process not only in permitting passage of steam and air as required by the process but also in not contributing any other inhibitory factors. For example they should not generate gases which could mimic the presence of retained air and restrict the penetration of steam.

Sterilizers for unwrapped instruments and utensils

C3.21 Sterilizers not intended for use with wrapped goods, for example bowl and instrument sterilizers, and small transportable electrically heated sterilizers rely on steam flow to remove air. Although the air may eventually be displaced from wrapped loads the process is slower and less predictable than when forced air removal is used.

C3.22 The only packaging suitable for unwrapped instrument and utensils sterilizers are “instrument orientation” trays which are constructed of open mesh or with sufficient ventilation holes to ensure that they present no barrier to air removal and steam penetration.

C3.23 BS 3970 Part 4 requires that load containers for transportable sterilizers should be designed to permit free draining of condensate and penetration of steam by perforation of appropriate surfaces. The perforated surfaces should have not less than 10% of their area as uniformly distributed perforations, each perforation being at least 20 mm^2.

Aqueous products in sealed containers

C3.24 Sealed glass or plastics containers containing aqueous solutions permit moist heat sterilization of the contents by virtue of the moisture present in the product.

C3.25 The container must have a gas-tight seal if the composition of the contents is not to be modified by evaporation of water from the contents or the ingress and condensation of steam from the sterilizer chamber.

C3.26 The container must be able to withstand the considerable internal pressures which will be generated during the sterilization process. This increase in pressure arises from the volumetric expansion of the container being insufficient to compensate for the volumetric expansion of the liquid, the increased vapour pressure of the liquid and the increased pressure of the heated air in the vacuity.

C3.27 The pressure generated in a correctly filled 1 litre bottle when it is heated to 121°C may exceed 8 bar.

C3.28 Plastic containers, particularly those made of polymers which undergo a reduction in tensile strength at the temperatures used for steam sterilization, are often only suitable for use in sterilizers which include air or gas ballasting to increase the pressure throughout the cycle and thus restrain the container from bursting. A similar approach may be used to sterilized devices used as packaging for example pre-filled syringes.

C3.29 The safety of operators will be at serious risk from the violent failure of containers and dispersal of their contents if the containers are removed from the sterilizer at too high a temperature (see SHTM 2010 Part 3 paragraph 14.20 d).

C3.30 The use of unsealed containers to avoid this problem is unacceptable. Not only is the composition of the contents subject to unpredictable changes, but liquids such as molten agar might still be boiling violently. Splashes from hot liquids of high thermal capacity can cause serious burns.

C3.31 Containers which are “unsealed” but plugged with porous material, or have the cap in place but left loose, that is not screwed tightly closed, may also become unsafe at elevated temperature. The evaporation of water from residues of the contents which boiled over during the early stages of the cooling process can effectively seal the container. It is important to emphasise that these are not theoretical considerations but represent a real hazard which has, in the past, caused injury to a number of personnel.

Low-temperature steam and formaldehyde

C3.32 The basic considerations for packaging for this process are similar to those for steam sterilizers for porous loads and wrapped goods.

C3.33 However, the thermal characteristics (both the thermal capacity and thermal conductivity) of the packaging can be of importance:

a. Materials which are slow to attain the required temperature may promote the polymerisation of the formaldehyde gas.

b. Materials of high thermal capacity promote the formation of excessive quantities of condensate which also may adversely affect the sterilization process.

C3.34 In addition, the extent to which the packaging material will absorb and adsorb both moisture and formaldehyde gas may affect the efficacy of the process.

C3.35 In general packaging should be kept to the minimum compatible with adequate protection for the product and the maintenance of sterility.

Ethylene oxide

C3.36 The packaging should be designed to allow removal of air and penetration of both steam and ethylene oxide and it should be demonstrated that the specified sterilization process does not affect adversely the functioning of the packaging.

C3.37 Impervious packaging materials are unsuitable for ethylene oxide sterilization.

C3.38 There are a considerable number of different ethylene oxide sterilization processes ranging from those employing pure ethylene oxide at sub-atmospheric pressures to those which use a mixture of ethylene oxide and carbon dioxide at pressures of several bar.

C3.39 The nature of the process, including the rate of air removal and the nature of the humidification stages used, will influence the suitability of packaging to be used in the process.

C3.40 A sterilization process that employs a high moisture content and several large and rapid changes in pressure may affect the strength of package seals, with a consequent loss of integrity, whereas. package seals of the same type would have been perfectly satisfactory for a process employing less extreme conditions.

C3.41 The extent to which the packaging absorbs moisture may have a major influence on the efficacy of the process and must be considered before a satisfactory humidification stage can be demonstrated.

C3.42 The extent to which the packaging absorbs or adsorbs ethylene oxide, and its permeability to ethylene oxide may have a major influence on the efficacy of the process and the subsequent aeration process used to remove the potentially toxic residuals.

C3.43 Process control is also a concern since packaging material that has become dehydrated may absorb excessive moisture during the conditioning phase; if this possibility was not recognised during validation the achieved cycle lethality may be adversely affected.

C3.44 The use of cartons (shelf packs, transit cartons) may be convenient for handling product but increase the post-sterilization level of ethylene oxide residuals, the necessary humidification time and the length of the gas exposure stage of the cycle (by inhibiting gas penetration). All the packaging which is intended to go into the sterilizer must be compatible with the process.

C3.45 The standard on validation of ethylene oxide sterilization processes (see EN 550) includes the requirement that the packaging specification be part of the definition and documentation of the sterilization process. The validation report should include or reference details of product sterilized, including packaging specification and load patterns in the sterilizer.

C3.46 It is therefore necessary that product used for physical and microbiological performance qualification studies should be packaged in an identical manner to that to be used routinely when they are presented for sterilization.

C3.47 The introduction of a new, or altered, packaging material or system requires validation. Physical and microbiological performance qualification studies should be performed on the introduction of new or modified packaging, although demonstration of equivalence to a previously validated package would satisfy this requirement.

C3.48 Many of the packaging materials for hospital use are the same as those for use in steam sterilizers because of similar permeability requirements; however, the lower temperatures involved in the process permit a wider range of materials to be used.

Hot-air sterilizers

C3.49 The thermal conductivity, specific heat and ability to withstand temperatures of 165°C, 175°C or 185°C (depending on the process used) for extended periods, without deterioration which impairs the utility of the packaging, are obvious considerations.

C3.50 The packaging does not need to be porous since the heat transfer normally takes place by conduction.

C3.51 However, in sealed packaging the contents of the pack when heated can exert a considerable pressure and may be sufficient to rupture the packaging material or its seals.

C3.52 Vented packaging systems that allow pressure equilibration may be suitable for use in hot air sterilizers which operate with a chamber atmosphere which has been filtered through a bacteria retentive filter. This is particularly important the during the post-sterilization cooling stage.

Irradiation

C3.53 The standard for validation of radiation sterilization processes (EN 552) requires that the process specification should include descriptions of the dimensions, density and orientation of the product within the packaging, as

well as the pattern for the loading of product within the container to be used to transport the packs through the irradiator. This should be established and documented before commencing performance qualification studies.

C3.54 The orientation of the product during irradiation is one of the factors ensuring uniformity of dose and the ability of the packaging to maintain consistent orientation of the product must be considered.

C3.55 The density of the packaging, and hence its “transparency” to the radiation to be used may be an important consideration, particularly in the case of electron beam irradiation.

C3.56 Although radiation sterilization is a low-temperature process there is nevertheless some increase in temperature above normal ambient temperatures and this should be considered.

C3.57 There is no requirement for the packaging to be gas permeable. If the packaging is gas tight it may reasonably be assumed to be a satisfactory barrier to microbial contamination.

C3.58 Many materials are structurally altered by the radiation process; they may become hardened and embrittled, or discoloured, for example.

C3.59 These radiation induced changes may be beneficial or disadvantageous to the subsequent performance of the packaging or they may simply be aesthetically unacceptable, for example the yellowing which occurs with some PVC materials.

C3.60 Many polymers are now available specifically formulated with stabilisers which make them suitable for use in irradiation processes. The adhesives used to seal packages must also be considered for potentially adverse effects of the radiation.

C3.61 For most hospital users, with only small numbers of items to be irradiated, the advice of the sub-contractor providing the irradiation sterilization service should be sought. Based on their experience of radiation sterilization of similar products they will often be able to suggest appropriate packaging which can be validated by comparison with previously validated products.

Compatibility with the labelling system

C3.62 The importance as labelling as an integral element of the product packaging has been stressed (see paragraphs C1.15 and C2.19 to C2.30).

C3.63 Labelling may take a number of forms, including:

- labelling printed directly on the packaging;
- printed labels attached to the surface of the packaging by adhesive, etc.

C3.64 Whether labels are printed directly on the packaging or onto discrete labels which are subsequently attached to the pack, the labelling system should:

a. not adversely affect the compatibility of the packaging with the sterilization process to be used, for example by excessively restricting the porous area available for gas exchange;

b. not be rendered illegible by the sterilization process to be used;

c. not employ ink of a type which may

(i) transfer to the pack contents;

(ii) react with the packaging to impair its utility;

(iii) change colour and render the label illegible;

(iv) interfere with the sterilization process by, for example, evolution of volatile components.

C3.65 Labels fixed to the surface of the packaging must be able to withstand exposure to the sterilization process and the defined storage and transport conditions without becoming detached.

C3.66 Given the low cost of computerised label printing systems there can be little justification for using hand-written labels with the inevitable variation in legibility that this causes.

C3.67 Writing on the packaging also presents an unacceptably high risk of causing damage to, for example, paper packaging, which may not be readily visible but is sufficient to breach the microbial barrier properties of the material.

Furthermore, some pens, such as ‘felt-tip’ pens and ‘marker’ pens, have inks which may release volatile components in sufficient quantities to interfere with the correct functioning of a steam sterilizer.

Compatibility with requirements for aseptic opening

C3.68 Failure to consider adequately how a pack is to be opened and the contents removed may significantly increase the chance of contamination occurring. With inadequate provision for aseptic opening a 10^{-3} probability of contamination is easily possible which compares unfavourably with a 10^{-6} probability of sterility required as a minimum standard before labelling a product as sterile (EN 556).

C3.69 The means of sealing or closing the pack should be tamper evident in order that the user may rely upon the integrity of the contents.

C3.70 For sterile products the other major consideration at the point of use must be the ability to remove the product from the packaging without it becoming contaminated with micro-organisms, in other words the aseptic removal of the product.

C3.71 The provision of aseptic removal may be influenced by a number of elements in the design of the packaged product including:

- the type of product;
- the packaging system chosen;
- the method of closure or sealing;
- the number of layers of packaging material;
- the arrangement of the contents of the pack;
- the use of special equipment to remove the contents.

C3.72 Sterile medicinal products include both parenteral and topical preparations. The former are predominantly aqueous solutions whereas the latter may be aqueous solutions, oils, emulsions (ointments or creams), or dry powders.

C3.73 The packaging system employed for sterile medicinal products will normally consist of a closed rigid or flexible container as the primary pack. This may be closed by being hermetically sealed or by being sealed with a penetrable (or removable) elastomeric closure (such as a bung, stopper or disk) held in place with a screwed cap or crimped overseal.

C3.74 Sterile medicinal products are usually best presented in single-use form. Where a multi-use presentation is employed there will be a requirement for a suitable preservative to be included in the product formulation.

C3.75 The primary pack may need to be overwrapped if it is necessary to provide for aseptic handling of the primary pack.

C3.76 Sterile medical devices may be presented as single items such as individual instruments, dressings, etc. or, as a single pack containing multiple items; the composition of which is designed so that contents comprise the items required for one (or more) particular procedure(s).

C3.77 These are commonly described in a variety of terms such as:

- Basic packs (dressing packs which may or may not contain instruments);
- Composite packs (instruments, dressings and other equipment/utensils);
- Supplementary packs (which include instruments, utensils, dressings for use with basic packs and composite packs);
- Procedure packs (which contain all the instruments, drapes, dressings and utensils required for a particular procedure);
- Linen packs (which contain all the drapes required for a particular procedure);
- Gown packs, dressing packs, etc.

C3.78 The packaging system employed for sterile medical devices may consist of flexible or rigid packaging, or the two types used in combination; and may

be intended for single use, or be re-usable or be a combination of single use and re-usable.

C3.79 These may be closed by heat-seal, adhesive, compression gaskets, or tortuous path closures. A common format used in hospital SSDs is a pack formed from a rigid tray wrapped in a flexible packaging material. The tray may be re-usable metal or plastic, such as polypropylene, or single use, such as metal foil, moulded pulp, folded cardboard.

C3.80 For medical devices the arrangement of the pack contents will be of importance. The contents generally are arranged so that when the pack is opened they are available in an order convenient to the user for the intended purpose and suitable for aseptic removal.

C3.81 The method of opening the sealed or closed pack and/or removing the contents affects the aseptic removal capability. The various sealing and closing methods may involve particular risks with regard to transfer of contamination from the outside surface of the pack, or to transfer of fragments of the packaging.

C3.82 Tortuous path seals formed by the folding of flexible packaging material may be constructed so that they may be opened without touching the inner surfaces.

C3.83 Pealable seals are used on heat sealed, and some adhesive-sealed, flexible packs and on many commercially produced packs, for example lidded blister packs. The construction of the seal should allow the opposing surfaces to be grasped easily and the seal on separating should not cause fibre shedding by, say, the splitting or tearing of either surface.

C3.84 Both flexible and rigid packaging systems are used which are intended to be broken, cut or torn open, for example ampoules, paper bags and pouches. It is important that this can be done without introducing contamination into the pack contents either from fragments of the packaging (for example glass particles from an ampoule), or from instruments used in the opening procedure, such as scissors for cutting open paper bags.

C3.85 Rigid re-usable containers for dry goods should have a tamper evident seal which must be broken before the container can be unlatched and the lid opened.

C3.86 Both single-use and re-usable containers for liquids, particularly those intended for topical administration or laboratory use, may have a seal which is formed from a compressible gasket (for example a rubber wad or stopper) held in place by, or as an integral part of, a screw capped lid. Aseptic removal of the contents will depend not only on the ease with which the cap and gasket can be removed but also on the method used subsequently to dispense the contents, for example pipetting, pouring.

C3.87 Both single-use and re-usable containers for liquids, particularly those intended for parenteral administration, may have a seal which must be punctured and penetrated by a suitable device to remove the contents, for

example using a hypodermic needle and syringe to remove the contents of a vial.

C3.88 The potential risk of introduction of contamination from surface of seal should be considered. The external surface of the seal may need protection (overseal) which can be removed immediately before use, or the instructions for use may require pre-treatment of the seal surface, for example by swapping with a 70% m/v aqueous solution of spore-free isopropanol.

C3.89 For re-usable systems the ability of the closure to re-seal after each penetration will be an important consideration in the maintenance of sterility.

C3.90 The seal for either single-use or re-usable systems must be of a material which will not be damaged by the penetrating needle to the extent that fragments of the closure will contaminate the contents of the container.

C3.91 Sealed packs should always be carefully inspected for seal integrity, or adventitious contamination, before being opened and this requirement should be drawn to the users' attention both in the labelling of the pack and on any instructions for use or training programme which may be given.

Compatibility with the contents

Medical devices

C3.92 The suitability of the packaging for use with the particular medical device should be established. This should include limiting values for physical characteristics of both the medical device as well as the stresses which will be imposed during sterilization and subsequent transport and storage.

C3.93 Factors to be considered include, but are not limited to:

- the mass and configuration of the medical device to be packed;
- the presence of sharp edges or protrusions;
- the need for mechanical and other protection;
- interactions with the packaging materials.

C3.94 Consideration of product interaction should also include physical contamination with the packaging material. Small particles introduced into the body during, for example, surgical procedures are widely reported to cause clinical problems including inducing adhesions, granulomata and foreign body reactions in tissues.

Medicinal products

C3.95 Factors to be considered include:

- interactions with the packaging materials, including adsorption, absorption and chemical reactions with components of the packaging

materials, for a period not less than the specified storage life under the specified storage conditions;

- adverse effects on the contents due to gas or water vapour permeability, such as permitting loss of water from a formulation, or permitting the ingress of oxygen and subsequent oxidation of one or more components of the formulation.

C3.96 Materials used for packaging should be compatible with the contained product. For example packaging intended for use with parenteral fluids should not shed particulate material to an extent which could compromise the quality of the parenteral being administered.

Laboratory products

C3.97 Factors to be considered include all those noted in the two previous sections for medical devices and medicinal products.

Toxicity

C3.98 Packaging materials and/or systems should not release material known to be toxic in sufficient quantity to cause a health hazard either before, during or after sterilization under the specified conditions of use.

C3.99 Evidence that the packaging material and/or system does not either contain material known to be toxic, or contain material which may react during the sterilization process to form a substance known to be toxic, in sufficient quantity to cause a health hazard is normally sufficient to meet this requirement.

C3.100 Manufacturers of packaging are aware of this requirement and should be able to provide evidence that the formulation of the packaging has been reviewed by a competent toxicologist and found to meet this requirement.

Biocompatibility

C3.101 The biocompatibility of the packaging should be assessed with regard to the intended use of the pack contents. If particular requirements for the product to be sterilized, for example freedom from particulate matter, cannot be established from the material specification for the packaging under consideration expert advice should be sought. In the first instance this advice should come from the manufacturer of the device, who has a legal obligation to specify any particular requirements for the safe sterilization of the product.

C3.102 Test methods for bio-compatibility are described in EN 30933-1; they require the services of a specialist laboratory.

Preservation of sterility

C3.103 The packaging materials and/or systems assembled in the form in which it will be presented to the sterilizers, when assembled, stored, transported and used in accordance with the producer's instruction, should preserve the sterility of the contents from the time at which they are rendered sterile to the expiry date specified by the manufacturer and/or the point of use.

C3.104 Preservation of sterility is achieved by preventing the ingress of micro-organisms. Many factors affect the probability of such ingress occurring. These include, but are not limited to:

- the concentration of micro-organism in the environment;
- the size of particle on which the micro-organisms occur;
- environmental conditions of temperature, humidity and pressure;
- the rate of change of these environmental conditions;
- flow rates through the layers of packaging material;
- pore size and other filtration parameters of the packaging material.

C3.105 There is no universally applicable, single test method which can be used to establish the microbial barrier properties of a pack.

For particular types or sizes of pack there are tests which may be of value as an overall monitor of microbial barrier properties.

C3.106 For most practical purposes it is necessary to infer satisfactory microbial barrier performance from a combination of tests designed to test attributes of the packaging which are related to microbial barrier properties, for example to test the gas tightness of seals.

C3.107 The time for which any packaging system will maintain the sterility of the pack contents is event related not time related. It is therefore necessary to define, and control, the conditions for both storage and transport, within which the pack will maintain the sterility of the contents.

Storage and transport of sterile packs

C3.108 It is necessary to ensure that the packaging is able to provide the protection necessary to maintain the performance characteristics of:

- the packaging during storage and transport under the specified conditions;
- the contents during storage and transport under the specified conditions.

C3.109 When handled according to instructions, the packaging should protect the product from physical damage and maintain the sterility of the medical device up to the point of use.

Number of layers of packaging material

C3.110 Products may be packaged in a single layer of packaging material, or in multiple layers. Multiple layers of packaging may be used to reduce the likelihood of contamination during storage and when the pack is opened.

C3.111 When two layers of packaging are used to facilitate aseptic removal of the contents:

- the outer wrap is sealed and acts as a barrier to microbial penetration to the product from the environment,
- the inner wrap may, or may not, be sealed and may, or may not, be intended to be a barrier to environmental microbial contamination. It acts as a protective cover during removal of the product.

C3.112 When the inner wrap is a microbial barrier it may serve to provide additional assurance of the maintenance of sterility.

C3.113 This inner wrap, having been maintained in a sterile state by the presence of the outer wrap, may be handled by persons, wearing sterile gloves and about to undertake an aseptic procedure.

C3.114 Moulded plastic shields covering hypodermic needles, plastic end-caps on intravenous administration sets are two examples of inner wraps found on commercially sterilized products. They may also serve additional functions unrelated to the sterile nature of the product, such as mechanical protection, protection of operators from hazards associated with the product etc.

C3.115 Double wrapping is essential for equipment that will be used in an aseptic environment such as an operating room or a protective isolation unit.

C3.116 In particular instances, triple-wrapped product may be necessary to permit the adoption of procedures with a high level of assurance that there will be no contamination, for example transfer of laboratory products into a sterility test containment facility or transfer of equipment and components into an aseptic manufacturing environment.

C3.117 Single wrapping may be more economical and appropriate when the product, although sterile, will not be used in an aseptic environment and will not be used parenterally or to penetrate tissue, for example Ryles tubes, oesophageal and suction tubes, urine bags, rectal examination sets etc.

C3.118 The various layers of packaging may be used to provide for different functional requirements, for example many surgical instrument and dressings packs are wrapped with an inner layer of paper or cloth which is used to provide a sterile field when opened onto a table, trolley or tray at the point of use.

C3.119 Two or more layers of packaging may be used together to provide a functional requirement which neither alone could meet, for example a single

layer of textile may not be an adequate barrier to microbial penetration but two layers in combination may provide satisfactory performance.

Primary and secondary packaging

C3.120 If two layers used together are needed to meet a basic performance requirement then layers both together constitute the primary pack.

Secondary packaging

C3.121 Several individual units, each wrapped in its own primary packaging, may be packed together in a “shelf pack” which may consist of a carton, plastic film wrap, film-wrapped carton or similar.

C3.122 For distribution, multiples of individual units or shelf packs may be packed in transit containers.

C3.123 These may be intended as single-use, for example fibreboard cartons or re-usable, for example plastic or aluminium boxes. Their primary function is to withstand the predictable risks arising during transport and distribution.

C3.124 Some or all of the secondary packaging may be applied before sterilization, especially in commercial sterilization. When this is the case the packaging, in its entirety as presented to the sterilization process, must meet the requirements for sterilization compatibility.

C3.125 When re-usable transport containers are employed, a documented and monitored procedure for maintaining them in a clean, hygienic condition and a good state of repair is necessary.

C4. Packaging materials and systems

C4.1 The following section summarises various packaging systems and materials that are available, including methods of effecting suitable seals or closures, their suitability for use with sterilization processes which may be employed by hospital users, and equipment necessary for their effective use.

C4.2 The summary is wide ranging and comprehensive, but not exhaustive. The absence of a particular system or material should not be taken as implying that it is unsatisfactory for use, nor should the inclusion of a particular system or material been seen as an endorsement of its use.

C4.3 The choice of suitable packaging systems and materials will be based on a number of factors. These include, but are not limited to:

- compatibility with available sterilization processes and other factors (see paragraph C3.5);
- particular requirements of the user;
- availability and cost of suitable automatic equipment for filling, sealing, labelling;
- availability and cost of suitable re-processing facilities for re-usable packaging;
- availability and cost of suitable disposal methods for used single-use packaging;
- standardisation of packaging systems within a single production unit.

C4.4 There is no one packaging system that is “correct” for all applications; and for any particular application there may be several systems available none of which is perfect. It may then be necessary to prioritise the requirements to be met by the packaging and select the system which most nearly meets these requirements (Table C2). The two characteristics which are afforded the highest priority most often are compatibility with the sterilization process and maintenance of sterility in storage and distribution.

Sterilization compatibility

Steam sterilization

Wrapped goods and porous loads

C4.5 Goods are normally double wrapped; at least one of the layers will usually be a sheet of paper, paper bag or paper/plastic pouch.

C4.6 The inner lining may be chosen primarily for its absorbency in order to retain condensate in a position from which it will be successfully evaporated during the drying stage of the sterilization cycle.

Table C2: Selection of packaging materials by sterilization process

Sterilization process	Re-useable packing	Single-use packing
Steam sterilization		
for wrapped goods and porous loads*	Containers(valves or filter) Textiles (cotton and/or synthetics)	Papers Plastic/paper pouches Cellulose/synthetic wraps Spun-bonded polyolefins up to 121°C
for instruments and utensils	Free-draining “instrument orientation” trays	
for aqueous fluids	Glass bottles Glass vials Plastic bottles	Glass bottles Glass vials/ampoules Plastic bottles Plastic pouches
Ethylene oxide	Containers (valve or filter)	Papers Plastic/paper pouches Spun-bonded polyolefins (eg.. Tyvek)
LTSF	Polypropylene boxes Open cell foam (for instrument protection)	Plastic/paper pouches Papers
Dry heat	Metal (eg.. Aluminium) canisters Glass containers	Metal foils Plastic films
Radiation		Treated paper Polyethlene Polypropylene Metal foils Various laminates Cardboard (PVC)

* the same packing materials are also suitable for use with LTS disinfectors

Fluids in sealed containers

C4.7 Glass or plastic bottles, vials or ampoules are used for rigid containers and plastic pouches, usually a laminated construction to optimise the performance characteristics, are suitable for flexible containers.

Dry heat

C4.8 Aluminium cans or tubes, glass tubes or jars, each of which may be sealed with push on caps, screw caps or crimp-on foil caps, are suitable for dry heat sterilization. Crimp-on foil caps with a pre-printed colour change indicator are also available.

C4.9 Items may be wrapped in heavy or light gauge metal foil or, for items such as laboratory glassware the foil may be used simply to seal the open end of the product.

C4.10 Plastic bags of the sort sold for roasting meat in domestic ovens may also be suitable.

LTSF

C4.11 Packaging may consist of paper, used as plain or creped wraps, or in the form of bags or, in combination with plastic film as pouches.

C4.12 Light cardboard boxes, or corrugated polypropylene boxes, adequately vented and overwrapped with paper or other material as a bacterial barrier are also suitable. When particularly delicate instruments are to be processed the use of an open cell foam for support and protection is acceptable.

C4.13 The quantity of packaging should be kept to the minimum possible.

Irradiation

C4.14 Polythene/polyester/nylon or metal foil may be used. The material may be non-porous and gas impermeable which gives good microbial barrier properties. Paper, spun-bonded polymers and non-wovens can also be used but lose the advantage of a process that can deal with impermeable packaging.

Ethylene oxide

C4.15 For ethylene oxide sterilization a high permeability to air, steam and ethylene oxide is essential.

C4.16 Paper bags or plastic/paper pouches are usually found to be most convenient for small articles. Wrapping in sheets of plain or crepe paper, or textiles, may be required for large procedure trays containing endoscopes or other thermolabile equipment.

C4.17 Moulded foam inserts may also be used to provide protection for sensitive equipment such as endoscopes.

C4.18 Polythene bags with gas exchange ports of Tyvek are also suitable.

Bacterial barrier properties

C4.19 The basic requirement is for a material which will not allow the product within the pack to be contaminated by the ingress of microbes in the environment from the time that it is removed from the sterilizer, during transport and storage up to the point of use.

C4.20 With a non-porous material, where gas flow through the material can only occur through diffusion, the material itself will be an absolute barrier to microbial contamination. The microbial barrier properties of the pack will then depend on the adequacy of the seal or closure. For example, an ampoule, if correctly sealed by fusion, and having no cracks or other flaws, will be an absolute barrier to microbial contamination.

C4.21 When a porous material is used the barrier to microbial penetration will not be absolute; there will be always a finite possibility of a micro-organism penetrating the barrier and potentially contaminating the pack.

C4.22 The probability of a micro-organism penetrating the barrier will depend on many factors, including, but not limited to:

- the rate of air flow through the web, which may be influenced by the rate and extent of environmental changes in pressure and temperature;
- the relative humidity, which can affect both the pore size and surface charge of natural fibrous materials (paper, linen etc.);
- the type and number of micro-organisms in the environment;
- the form in which they are presented, for example as single organisms or, as they are more usually found, on relatively large particles such as skin squames;
- the nature of the product, which may influence whether contaminating organisms can survive or multiply.

C4.23 The effect of these various factors is not the same for all materials. For example some porous materials are better at excluding particles of a given size at very low flow rates while other materials perform best at higher flow rates.

C4.24 It is apparent that the storage conditions will also be a controlling factor in the maintenance of sterility. Dirty, damp conditions can give rise to high microbial counts in the environment; large and rapid changes of temperature, and changes of pressure (including the slamming shut, or violent opening, of doors) will lead to an exchange of air between the contaminated air of the environment and the interior of the pack.

C4.25 The ability to maintain sterility is primarily “event related” rather than “time related”, although even under controlled conditions there is a greater probability of an adverse event having occurred after prolonged storage.

C4.26 The most sensitive time for contamination through porous wrapping material is when steam sterilized product has been removed from the sterilizer and is cooling down. During this process air will be taken into the warm and humid environment in the pack.

Materials used in packaging

C4.27 The materials of which the packaging is made will necessarily limit the sterilization processes with which it is compatible as well as affecting its ability to meet other performance requirements.

C4.28 Performance requirements for packaging materials include:

- permeability to air, steam and gaseous sterilants, (although this does not apply to materials intended for use with aqueous fluids in sealed containers, dry-heat sterilization by hot air or sterilization by ionising irradiation);
- resistance to penetration by micro-organisms from the surrounding environment;
- resistance to punctures, tears and other mechanical damage which would breach the barrier to microbial penetration;
- freedom from loose fibres and particles;
- freedom from toxic ingredients and non-fast dyes;
- compatibility with the contents under the proposed sterilizing conditions;
- compatibility degraded by with the sterilization process to be used, that is, not degraded by it.

Textiles

C4.29 Textile fabrics are used for packaging; traditionally these are woven cotton materials but may also be cotton/polyester blends.

C4.30 Specialist fabrics are also available which may are intended to be water repellent while at the same time being gas permeable. This may be achieved by several means, for example a particularly tight weave of polyester fibres, or a laminated construction with a middle lamella of a suitable polymer film. Care needs to be exercised in using these fabrics that the flow rate of both air and steam through the fabric is adequate for the sterilization process.

C4.31 Textiles are often used as a wrapping material for heavy packs, especially of theatre instruments, which are to be sterilized in a porous-load steam sterilizer.

C4.32 Textiles are stronger than paper, and stronger than many non-wovens, and will resist tearing and rupture.

C4.33 However, textiles are generally a less efficient bacterial barrier than sterilization grade wrapping paper and should always be used in two or more layers. The second layer may be a textile wrap also or a suitable sterilization grade wrapping paper. Alternatively, a sterilization grade paper bag may be used to enclose the textile-wrapped pack.

C4.34 Textile wraps are re-usable.

Papers and non-wovens

C4.35 Both papers, which are made from cellulose fibres, and non-wovens, made from a combination of cellulosic and synthetic fibres, may be used. Both types are suitable for porous-load steam sterilization and most gas processes because they are permeable to air, steam and other gases.

C4.36 The original papers used for steam sterilization wrappers were kraft papers produced for general purposes. Purpose made papers with better controlled porosity and microbial barrier properties, and with enhanced wet strength and water repellency are now used. These are available as plain sheets, creped sheets which give better drape characteristics, as bags and in combination with a plastic film as pouches (or reel material from which pouches can be made).

C4.37 Good drape and handle characteristics are also provided by crepe paper (BS 6254 1989).

C4.38 Plain papers may be used as wraps or preformed into bags or pouches. The bags and pouches may be plain sided or may be gussetted to accommodate bulky items.

C4.39 Wet strength and water repellency are specifically improved over “normal” papers by the impregnation of the paper with high wet-strength resins.

C4.40 The water content of the paper may be maintained at a relatively high level, thus improving the feel and drape of the paper and minimising superheating due to exothermal rehydration, by the addition of humectants such as sorbitol.

C4.41 Over many years experience the various forms of paper packaging have been demonstrated to provide an effective microbial barrier.

C4.42 Non-wovens are generally less effective as a microbial barrier and may need to be used in, or as one of, two layers; they are however generally softer with better handling and drape characteristics.

C4.43 British Standards exist for all the paper packaging materials and should be used as the basis for purchasing specifications. (These standards will be replaced in due course with European Standards currently in preparation; the draft standards cover the same range of requirements as the existing standards.)

C4.44 Non-woven materials, made from a combination of natural and synthetic fibres are also widely used. These are often used where otherwise re-usable textiles would be used. They are generally of greater porosity than paper wraps and for this reason may not be as effective as a microbial barrier. They have higher tear and puncture resistance and are softer with better drape qualities. They may also show extremely good water repellency.

Synthetic materials and laminates

C4.45 Polymeric materials, or plastics, may be used in the manufacture of rigid, semi-rigid, or flexible packaging systems.

C4.46 They may be in the form of sheet or film, which is non-porous, or be produced as a spun-bonded or non-woven sheet which is porous.

C4.47 Plastic materials are also used in the manufacture of moulded containers, for dry products or for liquids.

C4.48 Film or sheet material may be an absolute barrier to microbes if it is free from pinholes. Although it may be non-porous that does not necessarily mean that it will be impermeable. Most polymers have some permeability to gas, air, and water vapour. The extent of the permeability varies with temperature, concentration gradient of the diffusing substance etc. and although generally low may be important, for example in the long term storage and stability of a pharmaceutical product.

C4.49 Plastic materials are generally robust and resistant to tearing. The extent to which they show puncture resistance depends much more on the polymer and film thickness used. There have been in the past major problems with thin-film moulded polyethylene commercially produced packs being breached by the sharp edges of the product within.

C4.50 Plastic materials can usually be heat-sealed to give a high-integrity barrier.

Polyethylene (polythene)

C4.51 Polyethylene is effectively impermeable to air and water and is not suitable therefore for general use in ethylene oxide sterilization processes without special precautions. However very thin films (up to 0.076 mm) thick allow the passage of ethylene oxide (by dissolving in the thin film and then evaporating from the inner surface). Paper laminated with a thin polythene film may thus be used to provide a heat sealable paper for use in ethylene oxide sterilization.

C4.52 High-density polyethylene is produced as a spun-bonded, non-woven (known commercially as Tyvek) paper-like material. It is very tough, and although it is porous like paper it is water repellent.

C4.53 In commercial use it has been found to provide a satisfactory bacterial barrier. It is frequently used in packs which are to be ethylene oxide sterilized and may be used with a clear film in the form of a pouch, as venting panels in impermeable bags made of, for example polythene, or as a sealing lid on blister packs.

C4.54 It has also been found suitable for use in steam sterilizers operating at sterilization temperatures up to 121°C.

C4.55 It has some disadvantages in that it may attract dust and fibres owing to its electrostatic character, it can be difficult to print on and also it may be

difficult to seal, although these latter difficulties largely can be overcome by using non-oil based inks and lacquering with a suitable heat-seal lacquer, respectively. It is also expensive compared with paper.

C4.56 At temperatures above 125°C even high-density polythene has softened too much to be used on its own as an effective packaging material and it is therefore unsuitable for steam sterilization at 126°C or 134°C or for hot-air sterilization.

C4.57 Polythene can be sterilized by ionising radiation.

Polyester

C4.58 Polyester, in the form known as oriented or crystallised polyester, is used as a laminate with polythene in the construction of paper/plastic pouches and reel material.

C4.59 The polythene forms the inner surface which is heat sealed to the paper. The outer layer of the plastic laminate is polyester which gives the required mechanical strength at elevated temperature as well as a good printing surface.

Polyvinyl chloride (PVC)

C4.60 PVC generally has a very low stability to both heat and ionising radiation.

C4.61 PVC will absorb ethylene oxide in large amounts. This is exacerbated by the ethylene oxide combining with the phthalate plasticiser, from which it is aerated only very slowly under ambient conditions.

C4.62 Some grades of PVC are used for the moulded bases of commercially available blister packs.

Polypropylene and polycarbonate

C4.63 Both polypropylene and polycarbonate are relatively heat stable materials.

C4.64 Polypropylene has a very low permeability to air, moisture and ethylene oxide. It has been used extensively, either separately or in combination with other polymer laminates, as flexible, semi-rigid or rigid containers for heat sterilization of water and aqueous fluids.

C4.65 Polypropylene has been laminated with aluminium foil for use as packaging for wet or oily materials such as skin swabs, alcohol wipes.

C4.66 Polycarbonate has been used extensively for the manufacture of autoclavable laboratory bottles (at 121°C).

C4.67 Certain grades of polypropylene, specifically formulated for the purpose, can be radiation sterilized.

Nylon

C4.68 Nylon is heat stable, and is also steam permeable but it is impermeable to air. Packaging constructed entirely from nylon film is unsuitable for steam sterilization because the air retained in the package may interfere with effective sterilization. It may however be used effectively in combination with a porous material, such as paper, to form a steam-sterilizable pouch.

Glass containers

C4.69 Glass containers, are usually in the form of ampoules, vials, jars or bottles and come in a variety of capacities and shapes, with several different closure systems.

C4.70 Three different grades of glass are available.

a. Soda glass is normally the cheapest (also referred to as Grade I). It is subject to hydrolytic attack particularly when autoclaved containing aqueous solutions. Solutions sterilized in bottles made of soda glass may become contaminated with reactive silicates and show an increased pH. Such bottles are rarely intended for more than a single use.

b. Sulphated soda glass, also referred to as Grade II, is soda glass which is protected against hydrolytic attack by a surface coating of sulphate. The coating is normally applied by sublimation of ammonium sulphate onto the surface of the hot glass concurrently with annealing during the manufacturing process. Bottles made of sulphated soda glass are rarely intended for more than a single use and, if re-used, the sulphate coating is eventually lost and the glass is once again subject to hydrolytic attack.

c. Borosilicate glass, also referred to as Grade III, is much more resistant to hydrolytic attack than Grade I or II glass and is generally the preferred material for containers which are to be used for autoclaving aqueous solutions. Providing there is a suitable cleaning process compatible with the intended end-use, bottles made of borosilicate glass may be re-used a number of times.

C4.71 Borosilicate glass also has better thermal shock resistance characteristics than soda glass when used in a similar container.

C4.72 Glass containers may also be used for dry heat sterilization, and can withstand radiation sterilization. However, irradiation causes a darkening of the glass which may be aesthetically unacceptable.

Metals

C4.73 Metals are used in the fabrication of sterilization containers for use in both steam and hot-air sterilization processes, and to a lesser extent in gas processes such as LTSF or ethylene oxide. Since the material is neither porous nor permeable it must be constructed with a suitable venting system for use in sterilization processes other than dry heat or radiation.

C4.74 The choice of metal should be based on consideration of both its corrosion resistance to the sterilization process, for example in a steam atmosphere, and on its thermal characteristics. The ideal material would have a high thermal conductivity and a low heat capacity and would attain the required temperature quickly, uniformly and without the formation of excessive amounts of condensate.

C4.75 In practice, the choice is usually between aluminium, anodised or otherwise surface treated to give it suitable corrosion resistance, and a suitable grade of stainless steel.

Single-use packaging

C4.76 Both flexible and rigid packaging systems are available which are intended for single use.

C4.77 The recently enacted medical device regulations (see Chapter C2) include a requirement that sterile medical devices be designed, manufactured and packed in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market. There is thus a clearly stated preference for single-use packaging as the primary packaging for sterile medical devices.

Paper or textile wraps

C4.78 For wrapping materials two different folding methods have been adopted, both of which, when correctly executed, provide a suitable tortuous path to prevent the ingress of contamination.

C4.79 For large packs the parcel fold is the preferred method (see Figure C1).

C4.80 The pack contents are placed on the wrap, approximately in the centre of the wrap. The long edge of the contents should be aligned parallel to the long edge of the wrap.

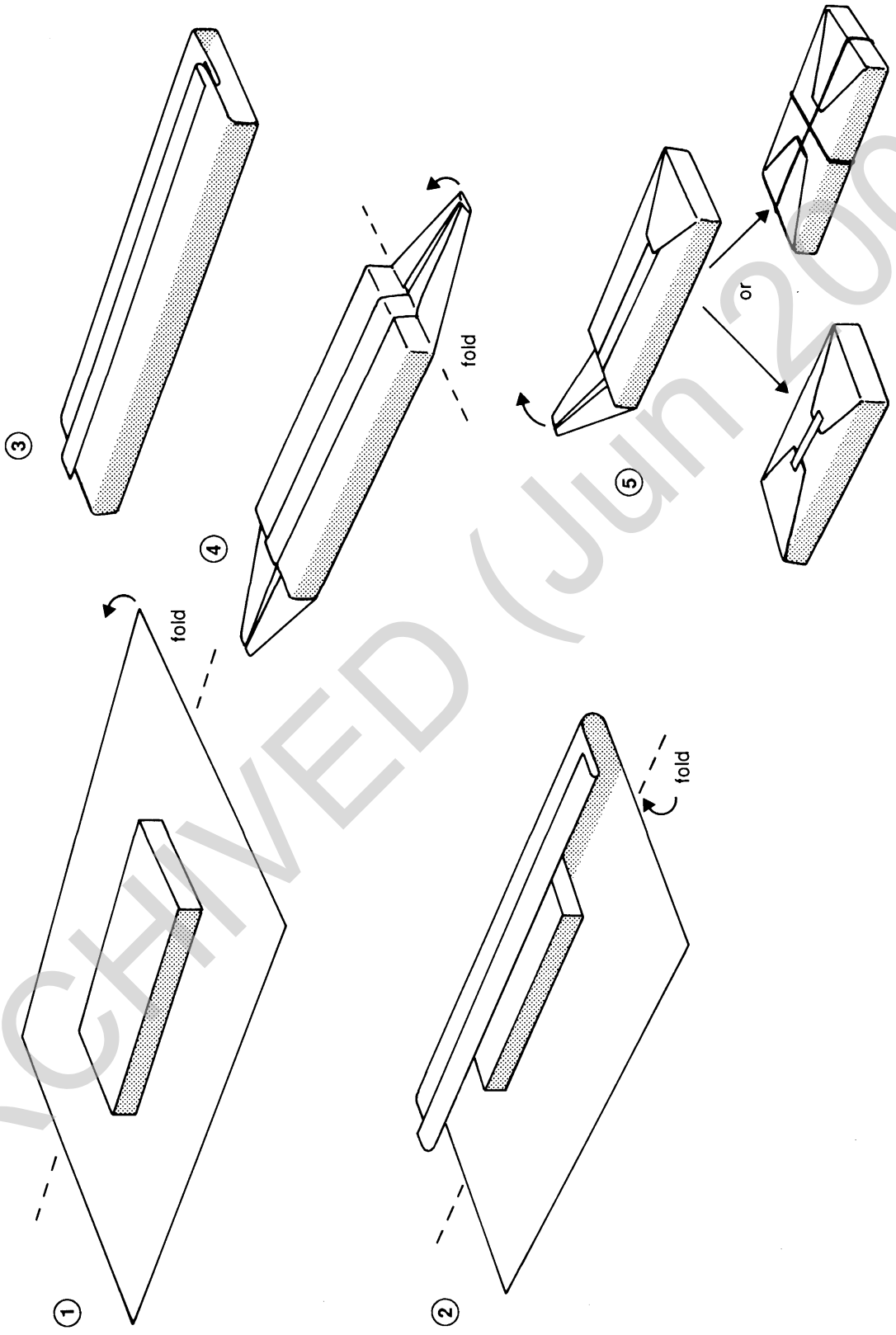
C4.81 One of the long edges of the wrap is folded over the pack contents to overlap the centre line, and the edge of the wrap is turned back on itself. The fold made by the turning back of the wrap should overlap the centre line of the contents.

C4.82 The opposite side of the wrap is then folded over pack contents to overlap the centre line (and the side already folded over the pack contents), and the edge is turned back on itself.

C4.83 The ends beyond the short side of the contents are then folded to a point and each is then folded over the contents.

C4.84 The same procedure may then be repeated for an outer wrap(s).

Figure C1: Diagrammatic representation of method for closing paper, non-woven or textile wrap using the parcel fold



C4.85 The wrap is secured in position using pressure-sensitive adhesive tape (high-temperature masking tape or autoclave indicator tape) or by tying with tape or cords.

C4.86 For smaller packs the envelope fold is preferred (see Figure C2).

C4.87 In the envelope fold method the contents are placed on the wrap diagonally and slightly off the centre line.

C4.88 The section of the wrap with the shorter corner-to-pack length is folded over the contents by bringing the corner to the centre.

C4.89 This is repeated with the corners to the right and left of the first folded corner.

C4.90 In each case the corner is turned back to provide a flap for opening.

C4.91 Finally the larger fold is brought over the top and tucked in under the earlier folds with a corner protruding, to facilitate aseptic opening.

C4.92 The envelope fold if properly executed is quite secure without further attention but if preferred may be secured also with tape or by tying.

Paper bags, paper/plastic pouches

Folding

C4.93 Folding is the simplest method to obtain a satisfactory closure for both pouches and bags, although it may not be convenient for high volume production (see Figure C3).

C4.94 The corners at the open end of the bag or pouch are folded diagonally to give mitred corners.

C4.95 The top of the bag or pouch is then folded over three times in succession and secured in place with a piece of high-temperature masking tape, or autoclave indicator tape.

C4.96 The folded top should always be secured with tape; staples should never be used because of the holes that are then made in the package.

C4.97 The folded top may be opened by cutting through the bag or pouch with a pair of sterile scissors. For non-critical applications it may be torn open; it should not be opened by removing the tape and unfolding the closure.

Self-seal

C4.98 Self-seal bags and pouches are closed by folding as described for plain top bags and pouches, above. However the bag or pouch is manufactured with an impact adhesive coating in a small area of the paper, which is protected before use by a piece of “release paper”.

C4.99 When the bag has been filled the top is folded over as previously described, the release paper is removed and the adhesive patch is pressed onto the surface of the bag to secure the folded top in place.

Heat seal

C4.100 Paper bags and paper/plastic pouches and reel material are available in forms suitable for heat sealing.

C4.101 The melting point of the heat-seal will effectively limit the maximum temperature at which the pack can be used. Heat-seal packaging should not be used at temperatures above those specified by the packaging manufacturer.

C4.102 Heat sealing is performed by compressing the opposing sides of packaging, coated on one or both inner surfaces with a lacquer, adhesive or polymer film, between heated plates.

C4.103 Packaging intended for heat sealing may be film coated, grid lacquered, or have an adhesive band.

C4.104 Film-coated heat-seal packaging has a thin film of a suitable polymer, such as polythene, laminated to the inner surface. When heated this melts sufficiently to fuse with the opposing surface and form a seal. The heat-seal polymer may be laminated to another plastic or to paper. The polymer film, if applied to the paper element, may limit the porosity of the pack.

C4.105 Grid-lacquered heat-seal packaging has one side, usually the paper, printed with a heat-seal adhesive in a repeating diamond pattern all over the inner surface. Care needs to be taken that the width of the heat-seal is sufficient to ensure that there is a continuous seal across the width of the packaging.

C4.106 Adhesive-coated heat-seal packaging has a band of heat-seal adhesive printed on the inner surface of the packaging in the area where the heat-seal is to be made. The adhesive is coloured, usually blue, to aid identification of the heat-seal area.

C4.107 The seals need to be peelable. They should peel without splitting, tearing or shedding paper fibres since fibres can cause adverse reactions if introduced into open wounds.

Figure C2: Diagrammatic representation of method for closing paper, non-woven or textile wrap using the envelope fold

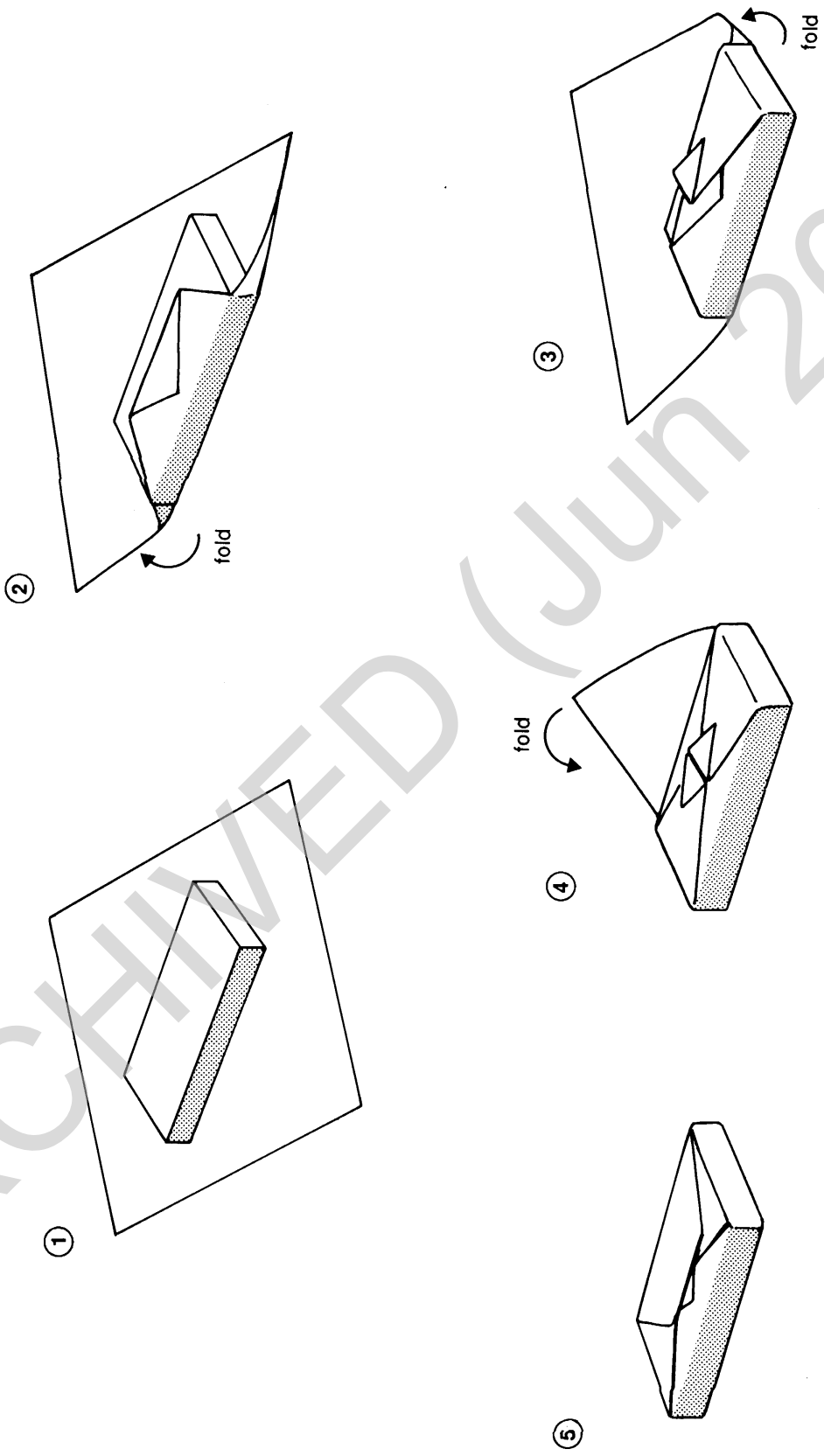
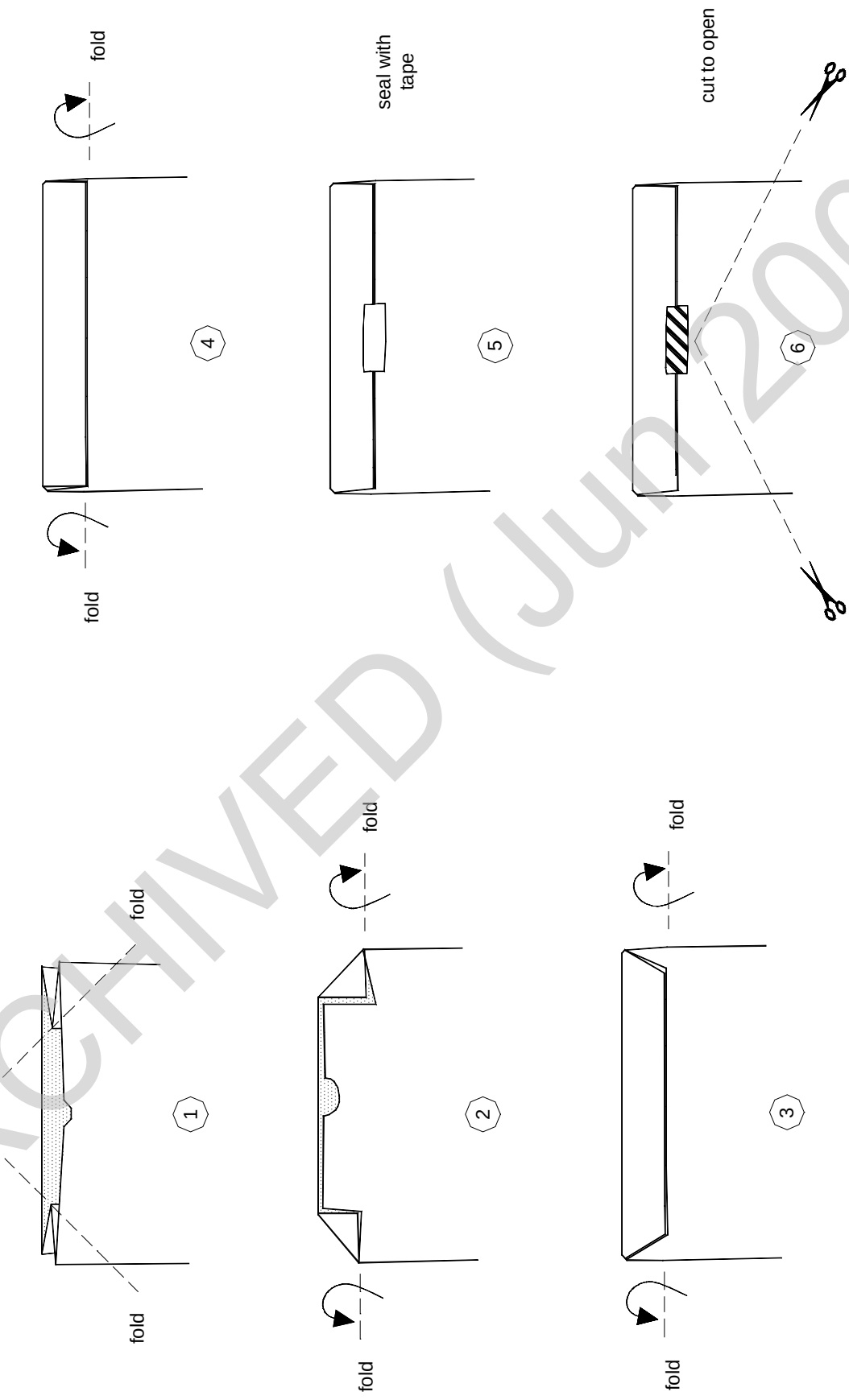


Figure C3: Closure method for plain top sterilizer bags



C4.108 Peelability is a compromise between seal strength and the peel characteristics required which can only be achieved by use of the correct heat-sealing conditions.

C4.109 The heat-seal may be a single line, in which case it should be not less than 5 mm deep and extend across the width of the pack, or a series of lines each about 1 mm wide and 1 mm apart to give a seal width of about 9 mm, with each line extending across the full width of the pack.

C4.110 The heat-sealing process must be undertaken with care. Creases in the packaging material can result in inadequate or uneven seals.

C4.111 A weak point in the heat-seal of paper bags may often be found in the corners where the paper is folded back on itself and in gusseted packs where four thicknesses of material become two. This latter problem can be minimised by reverse folding the gusset in the area to be heat sealed, before sealing.

C4.112 The effect of the sterilization process on heat seals must be considered. The elevated temperatures involved in steam sterilization can weaken the seals. Ethylene oxide gas leaves many seals unaffected but can cause embrittlement of others.

C4.113 Heat sealing is not only used for flexible packaging. It may be used also on rigid packaging when lids are sealed onto moulded plastic bases. The base tray may be moulded in-line just before filling or may be pre-formed. The lid may be of paper, Tyvek or other porous material for use in steam or gas sterilization processes or of impermeable film for use with radiation sterilization.

Glass containers

C4.114 Bottles and vials are extensively used for aqueous solutions for use as topical and parenteral medicines, microbiology media, laboratory reagents, in vitro diagnostics, disinfectants, etc. which are to be sterilized by moist heat.

C4.115 Glass containers may also be used for hot air sterilization of non-aqueous liquids, such as oils.

C4.116 Containers should never be filled with a volume greater than the manufacturer's recommended maximum.

Ampoules – fusion seal

C4.117 Two forms of glass ampoule are available; one form intended only for automatic (or semi-automatic) filling and sealing and one which is suitable for manual sealing.

C4.118 Ampoules intended for automatic filling and sealing may be supplied, internally clean, sterile and apyrogenic, with the neck closed by a “bubble” of glass. During the automatic filling process this “bubble” is melted by a flame directed vertically downwards to open the ampoule immediately prior to filling. This normally takes place in an environment controlled to be free from contamination. This type of ampoule is not suitable for manual filling and sealing operations.

C4.119 The relevant DIN standards may be used as suitable specifications.

C4.120 Ampoules are sealed by fusion. After filling, the neck of the ampoule is heated, almost invariably in a gas flame, until the glass softens and the walls of the neck coalesce, surplus unmelted glass in the neck above the point of melting is drawn away and the fused end of the neck is allowed to cool.

C4.121 For any given design of ampoule, the temperature of the flame, the duration of heating and the time and speed at which the surplus neck material is drawn off all affect the quality of the seal. When correctly performed the seal is as strong, or stronger than other parts of the ampoule.

C4.122 Ampoules for use in freeze driers are similarly sealed by fusion.

C4.123 Ampoules are opened by breaking off the neck. This may be facilitated by the inclusion of a deliberate weak point, in the form of a break ring, at the base of the neck during manufacture. Other methods which are available include notching the neck of the ampoule with a glass file, creating a fracture line by the application of a hot wire or rod and several commercially available devices.

C4.124 Whichever method is to be employed, users should be given appropriate instructions and training and should always take precautions to protect their hands from injury due to broken glass.

C4.125 Ampoules are produced to a high level of consistency and faults in sealing are likely to be due to poor setting up or control of the sealing method and rarely, if ever, due to variations in the ampoules.

C4.126 After the ampoules have cooled, careful visual examination, preferably using a magnifier and a polarised light source, should be used to inspect the seal and any showing cracks, thinning or “blowing” of the seal and sharp protrusions or “tails” of glass, should be rejected.

C4.127 A vertical drop of 10-15 cm, for example inside a tube of suitable diameter so that the sealed end impacts onto a solid surface, such as a plastic laminate, may also be used to test the ampoule seal. A satisfactory seal will survive, whereas a weak seal will break.

Vials and bottles

C4.128 As manufactured, glass bottles are generally clean, sterile and apyrogenic. Nevertheless they should be washed before use since they may have become contaminated during packaging and distribution, unless special precautions were taken to avoid this happening.

Screw caps

C4.129 Screw caps may be made of metal or plastic. They may be used to used to retain in place a separate elastomeric seal, such as a stopper or a wad, or they may incorporate a seal within the cap. In either case the seal is formed by compression of a deformable sealing material between the cap and the glass container. The compressive force applied is a key factor in creating a leak-tight seal.

C4.130 Metal caps may “back-off” during autoclaving. The differential thermal expansion of the metal of the cap and the glass of the bottle combine to make the cap unscrew slightly during processing. This rarely happens with plastic screwcaps.

C4.131 The problem can be minimised for metal caps by careful control over the extent to which the cap is tightened before sterilization.

C4.132 Devices to control the force used to tighten the cap (torque) should be used both to ensure reliable sealing and to minimise the risk of overtightening which can damage the cap or make it difficult to remove.

Crimp caps

C4.133 Crimp caps are metal, or sometimes plastic, capsules used to retain an elastomeric seal, usually in the form of a stopper, in position in the neck of the container.

C4.134 During the application of the crimp seal, pressure is applied to compress the stopper slightly against the top surface of the neck finish of the bottle. The skirt of the overseal is bent under the base of the retaining rim on the bottle neck by the crimping device. This retains the stopper in place and maintains it under slight compression to provide a good seal.

C4.135 During steam sterilization of the sealed container the pressure applied by the crimp may be released to some extent by the thermal expansion of the metal capsule. This, and the high internal pressure generated within the container, may cause the seal to leak. It should not be assumed that a seal which is demonstrably leak tight at room temperature will remain so throughout the various stages of steam sterilization.

Re-usable packaging

Textiles

C4.136 Textiles are used in combination with aluminium trays for packs of theatre instruments.

C4.137 The textile wraps should be laundered before each re-use.

C4.138 Control should be exercised over the laundry process to ensure that fabric softeners and fresheners are not used since many of these contain volatile components which will evolve gas during steam sterilization and compromise the efficacy of the sterilization process.

C4.139 The importance of thorough inspection before re-use cannot be over-emphasised. A light table should be used, and wraps with pinholes, clearly visible as points of light, should not be used.

C4.140 The location of the defect should be clearly marked and the item sent for repair by means of a heat-seal patch. Sewn patches are not acceptable because of the needle holes created around the patch.

C4.141 Worn textile wraps are readily discernible since the light will shine through the more open weave that occurs as the fabric wears. These should no longer be used as a sterile packaging wrap.

Containers for solid goods

Impermeable or unvented containers

C4.142 Aluminium tubes with crimped foil caps and larger canisters (made from aluminium, copper or stainless steel) with slide or screw-fit caps may be used satisfactorily for hot-air sterilization. Containers of this sort are used frequently for pipettes or glassware in the laboratory.

Open-topped trays and perforated containers

C4.143 Trays for containing sets of theatre instruments, or similar, are often constructed in aluminium. Plastics such as polypropylene may also be used. The trays may have solid bases and sides or be equipped with drainage ports to allow condensate formed during steam sterilization to run off.

C4.144 When condensate drainage is provided it is necessary to ensure that the condensate is not discharged onto other parts of the sterilizer load, which will then emerge from the sterilizer wet.

C4.145 Trays may be overwrapped in textiles, single-use wraps or bags, or a combination of these materials to achieve the required protection, absorbency and microbial barrier properties.

Instrument orientation trays

C4.146 These trays, usually constructed in metal, are fitted with retaining clips designed to hold a particular set of instruments in position. They are often found in dental practice and also for use with sets of orthopaedic instruments and rigid endoscopic instruments.

C4.147 They are almost invariably fully vented, or unlided, and in this condition may be suitable for use in a steam sterilizer intended for unwrapped instruments and utensils (see paragraph C3.23).

Dressings drums

C4.148 Perforated metal containers, fitted with a filter material and closable louvres were specified in BS 3281, 1960, for use as “dressings drums”. These were intended to contain dressings and porous goods sufficient for a number of clinical procedures. The product has been regarded as obsolete except for its use, until recently, as a convenient container for towels for the Bowie and Dick test. Even this use has now been discontinued.

C4.149 There is, however, a new generation of re-usable rigid containers intended for use as a packaging system in steam (and in some cases, gas) sterilization processes. These are intended to contain instruments and/or porous goods which will be used in a single clinical procedure. They are thus more akin to the trays described in paragraphs C4.143 to C4.145 than to the obsolete dressings drums.

Re-usable rigid containers

C4.150 A European standard specifying performance requirements for rigid re-usable containers is in preparation. When adopted it will be published as BS EN 868 – 8.

C4.151 Container systems are constructed in a variety of materials and those from various manufacturers differ greatly in design, construction and mode of operation.

C4.152 The containers are constructed from impermeable materials. The joint between the lid and the base is sealed by means of a suitable gasket, which should be accessible for inspection and cleaning between uses.

C4.153 In order to permit the flow of gases (air and steam and, where applicable, sterilant gas) in and out of the container that is required by the sterilization process the containers are fitted with one or more sterilant ports.

C4.154 Two different operating principles are used for the sterilant ports, although both may be used in combination. The exchange of gases may be through a porous filter material or through a valve system.

C4.155 The filter system is little different in principle from the porous packaging systems considered previously. Its compatibility with the sterilization process depends on its porosity and on being able to provide the necessary flow rate through the filter to permit attainment of the sterilizing conditions within the container.

C4.156 The ability to maintain sterility depends on the filter efficacy and whether it is able to exclude particles of a size which may contain viable organisms. The small area of surface available compared with the volume of the pack produces relatively high flow rates across the filter material and this influences the materials which can be used effectively.

C4.157 If a re-usable filter is used then great care is needed to ensure that:

- it has not become partially blocked, thus impairing the flow of gases and compromising the sterilization process;
- it has not been damaged, thus allowing the passage of unfiltered gases which would compromise the maintenance of sterility.

C4.158 Both re-usable and single-use filters need to be installed correctly so that the filter is effectively sealed in the holder and there is no passage of unfiltered gases around the filter.

C4.159 The alternative system for sterilant ports is the valve system.

C4.160 Outside the sterilizer the valve is normally closed and, if the seals on the valves are effective, presents an impermeable barrier to external contamination.

C4.161 The valve system has to be arranged to open automatically in the sterilizer to permit the exchange of gases between the container and the environment.

C4.162 A number of systems are used by the various manufacturers but most depend on valves which open in response to a pressure difference between the container and its surroundings. A diagram of the operation of such a system is shown in Figure C4.

C4.163 It is apparent that a finite pressure difference must exist across the valve before it will open. The magnitude of the pressure difference will depend on the force exerted by the springs keeping the valve closed.

C4.164 If the pressure difference required to open the valve is too great, the contents of the container will not be exposed to the sterilizing conditions in the sterilizer chamber. The correct functioning of the container is closely related to the pressure change characteristics of the sterilization cycle.

C4.165 If the required pressure difference is too small the valve will open outside the sterilizer due to changes in ambient pressure and temperature, thus allowing the inflow of unfiltered air from the environment.

C4.166 Some container systems are also fitted with a valve in the base of the container which is used to allow condensate to drain away, to assist in drying the contents of the container.

C4.167 The condensate drain valve may be fitted with a thermostatic device to open the valve when it is above a specified temperature, say 80°C, or it may operate on pressure differential as previously described for valved sterilant ports.

C4.168 After repeated use, the springs controlling a valved system will age and the force exerted by them will change. It is essential that the manufacturer's instructions for maintenance, testing and replacement of key components such as seals, sterilant ports and drainage valves are followed rigorously.

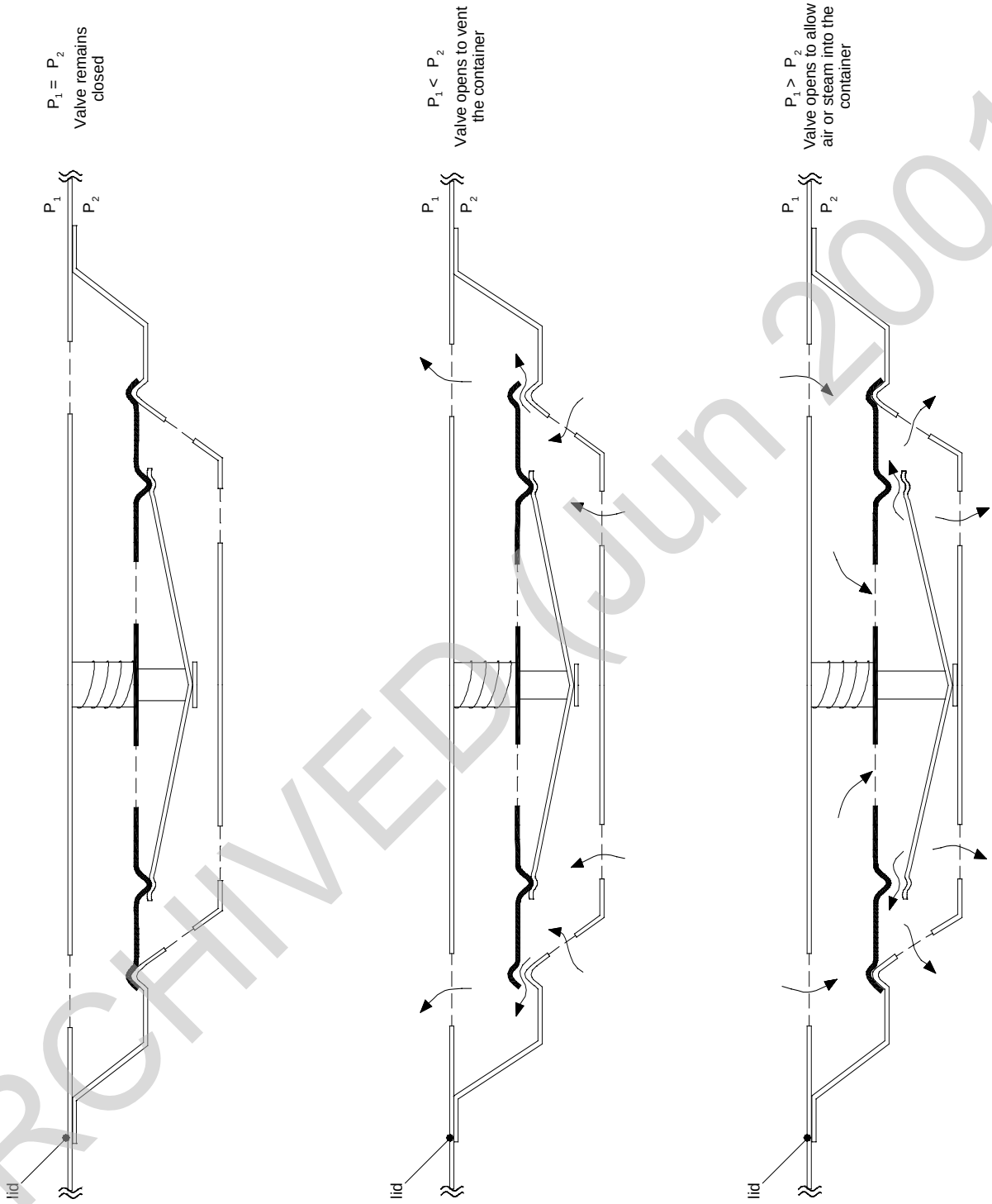
C4.169 The performance of either type of container may be seriously affected both by the nature of the sterilization cycle (particularly the characteristics of the air removal phase and the drying stage) and by variations in the quality of services supplied to the sterilizer (for example the dryness fraction of the steam). These variables are sterilizer and site specific respectively.

C4.170 It is necessary, therefore, to establish, by appropriate on-site testing, that any particular design which it is intended to use functions correctly in the specific sterilization cycle with which it is to be processed, in the sterilizers which will be used in practice.

C4.171 Re-usable containers have a number of apparent advantages. They offer excellent mechanical protection to the contents and a convenient, modular system for storage and distribution.

C4.172 The use of a solid-walled container gives the impression of providing good protection against microbial and other environmental contamination. In practice the barrier properties are dependent on the adequacy of gaskets and seals and the sterilant ports described above.

Figure C4: Diagram to show the principle of operation of value-type re-usable container systems



NOTE: The above diagrams are intended to be an idealised example of the operation of a valved system. They do not represent any commercially available system.

C4.173 The condition and function of filters, valves, sealing gaskets and locking systems needs to be verified on each container before each use.

C4.174 Between uses containers should be disassembled and cleaned following the manufacturer's recommendations. These usually suggest cleaning by washing with a mild detergent, either manually or in a washer/disinfector.

C4.175 The choice of detergent should accord strictly with the manufacturers recommendations since a number of cleaning agents in common use can cause corrosion or surface cracking on the metal or plastic surface of containers.

C4.176 These containers are often used to return used and soiled instruments, which are potentially contaminated. Whenever practicable they should be decontaminated and cleaned in a washer/disinfector.

C4.177 Most containers are fitted with interior baskets or mesh trays used to hold the instruments. These may be suitable to contain returned instruments as they are processed through a washer disinfector.

C4.178 In use the containers need to be properly loaded if they are to be used successfully. The manufacturers recommendations concerning the maximum weight, the proportion or density of metal ware or rubber goods and the presence and location of absorptive materials in the load should be followed.

C4.179 Some containers are intended to be used in conjunction with porous packaging materials, either as an inner or outer layer of packaging, whereas others are intended to be used, and will only function correctly, without any other packaging being present during sterilization. It is important that the manufacturer's instructions are followed.

C4.180 Containers which are not intended for use with a second layer of packaging, that is those which can only function as a single packaging layer, are not suitable for use in an aseptic environment (see paragraph C3.111).

C4.181 Containers manufactured to the proposed European Standard will be sized in relation to the standard loading module for large steam sterilizers (see EN 285). High packing densities within the sterilizer chamber can be achieved and it is important to ensure that the maximum permitted load for the sterilizer is not exceeded.

C4.182 To avoid problems with moisture retention within the container it may be necessary to increase the time allowed for the drying stage of the sterilization cycle.

C4.183 Each container should be fitted with a tamper evident closure system which should provide a clear indication when the integrity of the closure has been compromised.

C4.184 The containers are designed to stack for storage purposes. Containers from any one manufacturer should stack securely but containers of different provenance may not.

C4.185 When purchasing this type of packaging system all the containers should be from the same manufacturer to ensure compatibility.

C4.186 Re-usable containers are often promoted on the basis that they are more cost effective than single-use packaging. A decision based on cost grounds requires careful evaluation of the initial capital cost, cleaning and maintenance costs (including all equipment, components, consumables and labour required), the working life (the number of re-uses) which the manufacturer is prepared to guarantee, the likelihood of damage or loss and the cost of eventual disposal.

Glass containers

C4.187 Bottles intended for single use should not be re-used. Bottles intended for multiple use are available for most applications.

C4.188 Re-usable containers should not be used for solutions intended for parenteral administration.

C4.189 The information given for single-use screw cap and crimp-on closures is equally applicable to re-usable containers, with the following additional requirements.

Vials and bottles

Cleaning

C4.190 Before bottles can be satisfactorily re-used a cleaning procedure is required which has a demonstrated capability to remove any dirt or contamination, as well as any residues from the previous use. It is also important that the cleaning process is well controlled and ensures that there are no residues of cleaning agents.

C4.191 Cross-contamination can be most easily controlled by ensuring that whenever possible re-usable containers are only refilled with the same product, for example by reserving a set of bottles only for sterile water and another set only for sterile isotonic saline and so on.

Inspection

C4.192 Inspection of the bottles after cleaning and prior to re-use should include a careful visual examination of the neck finish. A chipped or cracked neck finish could prevent an adequate seal or lead to the failure of the seal during transport or storage. Bottles that have been damaged in this way should be scrapped.

C4.193 Inspection of the outer surface of the bottle should also be made. Bottles being sterilized are subjected to considerable stress both from the high internal pressures generated and from thermal shock. Scratches or other mechanical damage on the outer surface of the bottle weaken it and significantly reduce the pressure and the thermal shock which can be tolerated without breakage.

C4.194 One bottle breaking in a sterilizer load may provide sufficient force to cause others to break also. Re-usable bottles with surface damage should be rejected and either used for applications which do not require steam sterilization or be scrapped.

C4.195 The inspection of the neck finish should also consider any damage to the screw threads or the retaining shoulder on the outside of the neck of bottles which are closed with screw caps or crimped seals respectively.

Screw caps

C4.196 Screw caps, and the elastomer wads, stoppers or bungs used in conjunction with them, are often regarded as re-usable, and many of them may be satisfactorily re-used a number of times.

C4.197 The screw cap should be separated from any sealing wad and both should be thoroughly cleaned and inspected for damage before re-use.

C4.198 Metal caps that have been dented, or are showing visible signs of wear on the threads, should be scrapped.

C4.199 Rubber wads and rubber stoppers should also be carefully inspected for surface damage and any showing cuts, abrasions, staining or permanent deformation should be scrapped.

C4.200 Plastic screw caps with a built-in seal are also commonly used. These should be inspected very carefully for damage to the thin sealing gasket which is moulded into the inner surface of the cap. Any damage to this area will almost certainly cause the cap to leak.

Crimp caps

C4.201 Crimp caps are not themselves re-usable but the bottles on which they may be used can be. A special tool and some care is needed to remove crimped seals without risk of injury.

C4.202 The old seal should be discarded. The seals are usually fabricated from aluminium and the metal can therefore be reclaimed.

C4.203 The elastomer seal should also be scrapped.

C5. Purchase, quality control and storage

C5.1 The purchase, handling and control of packaging materials should be given similar attention to that given to components and other materials incorporated directly into the product.

Purchase

C5.2 All packaging materials should be purchased, whenever possible, to a British Standard or other suitable specification from approved suppliers.

C5.3 Packaging material should be purchased only to an agreed, written specification. When it is intended to purchase a catalogue item, the specification for that item should be obtained from the supplier and used as the basis of that purchase, and all subsequent purchases of the material. This should ensure that the user is informed of any changes in specification subsequently made by the supplier.

C5.4 The purchase order should be based on not more than the quantity which can reasonably, be expected to be used within the manufacturer's stated shelf life for the product.

C5.5 Although paper products, and other packaging materials, have a prolonged shelf life the manufacturer's expiry date may relate to other properties of the product such as a process indicator or a heat-seal adhesive whose performance may deteriorate on storage.

C5.6 The specification and purchase order should require that the material be delivered in unopened containers, using covered vehicles, suitably protected from water damage or soiling and that it is handled with care to prevent mechanical damage.

C5.7 The packaging materials should be supplied suitably wrapped to provide the required protection when it is stored under the specified conditions.

Specification

C5.8 For medical devices and medicinal products, and generally for laboratory products also, the specification should include:

- a description of the materials including:
  - the designated name and any code or reference;
  - the size;
  - the quantity in each unit pack delivered;

- the reference, if any, to a pharmacopoeial monograph, British Standard or other published specification;
- the approved suppliers, and if possible, the original producer of the material;
- a specimen of printed materials;

- directions for sampling and testing, or reference to written procedures;
- qualitative and quantitative requirements with acceptance limits;
- storage conditions and precautions including the maximum period of storage.

Quality control

C5.9 In many cases users of packaging materials will lack the facilities necessary to carry out a comprehensive independent assessment of delivered materials for conformity to their purchase specification.

C5.10 Nevertheless every reasonable step should be taken to establish conformity. This requires that each delivery should be examined to ensure that:

- there is no visible damage to the shipment;
- the delivery note, the label description and the purchase order are in agreement concerning the quality, size and number of the material;
- that each consignment has clearly identifiable lot numbers;
- that each lot delivered is accompanied by a Certificate of Analysis or Certificate of Conformity, or if the delivery is a further supply from a lot previously received that the appropriate certificate is on record.

C5.11 When, due to the nature of the packaging or the product, it is necessary to carry out tests, other than a careful visual appraisal, on incoming packaging materials a random sample should be taken and submitted for analysis.

C5.12 There should be a formal sampling plan which should take account of:

- the quantity received;
- the quality required;
- the nature of the material, and the risk involved if the material is not to specification, for example if the product makes contact with the packaging material;
- the established reliability of the packaging manufacturer.

C5.13 The number of samples taken should be specified statistically, in accordance with a recognised standard, such as BS 6000 or BS 6001.

C5.14 In confirming that the material supplied is identical in every respect with the material ordered particular attention should be paid to printed labels and packaging materials.

C5.15 A system for segregating delivery of packaging materials which have not been examined from those which have been found suitable for use should be implemented.

C5.16 Provision should be made for the temporary secure storage, prior to disposal or return to the supplier, of material which was delivered but, on examination was found not to conform to the specified requirements.

Storage

C5.17 Packaging materials should be stored under conditions which are maintained within those specified by the manufacturer of the packaging. This is best achieved by environmental control of the storage area.

C5.18 The temperature, and where necessary the humidity, of the storage environment should be monitored with a maximum-minimum thermometer and hygrometer, even if the store is not environmentally controlled.

C5.19 Paper and other moisture sensitive packaging materials should not be stored adjacent to:

- external walls or other surfaces which may be at a lower temperature than the ambient temperature of the store;
- sources of heat which could cause dehydration of the packaging material.

C5.20 Sheet materials should be stored flat, not on edge.

C5.21 Packaging materials should be stored on shelves, clear of the floor.

C5.22 Pre-printed labels and other printed packaging materials should be stored in secure conditions which exclude unauthorised access and should be transported in separate containers in order to avoid mix-ups.

C5.23 Packaging materials should be issued for use only by authorised personnel following an approved and documented procedure.

C5.24 Outdated or obsolete packaging material, especially printed material, should be destroyed and this disposal recorded.

C6. Validation of packaging systems

C6.1 All materials and procedures for packaging should be specified in documented form.

C6.2 Before a particular packaging system is adopted for a product, or group of similar products, it should be evaluated to establish its suitability.

C6.3 This evaluation should be documented.

C6.4 Specific testing may not be necessary when appropriate data are available, historically from similar use (whether by the same or different sterile product manufacturers), from the manufacturers of the packaging system or from an independent third party.

C6.5 The factors that need to be considered for evaluation include, as a minimum, those listed in paragraph C3.5.

C6.6 The compatibility of the packaging with the sterilization process can be established for many packaging systems by demonstrating conformity of the packaging and the sterilization process with published standards, for example sterilization-grade paper bags manufactured in conformity to BS 6257 for use in a sterilizer conforming to BS 3970 Part 3 and operated in accordance with the guidance given in this SHTM may be presumed to be compatible.

C6.7 Re-usable containers should be subjected to thermometric performance tests before they are adopted as a packaging system. This may be accomplished using a container modified to provide a gas-tight thermocouple entry port and carrying out tests essentially similar to the small load and full load tests described in SHTM 2010 Part 3 paragraphs 13.7 to 13.14 and 13.15 to 13.24 respectively.

C6.8 The tests should be carried out with a container fully loaded with items of the type which it is intended to process. If both instruments and textiles are to be processed the container should be tested under both fully loaded conditions. The full load test should be carried out with the sterilizer fully loaded with fully loaded containers.

C6.9 The temperature profile obtained should not show any delay in the contents of the container equilibrating with the sterilization temperature in the chamber, when compared to the results obtained using a small-load test pack.

C6.10 Load dryness should be verified using either the hospital load test described in SHTM 2010 Part 3 paragraph 13.37 or, when quantitative results are necessary, by a modification of the method described in SHTM 2010 Part 3 paragraphs 13.25 to 13.36.

C6.11 The compatibility of the packaging with the labelling system will usually be established by using the labelled pack for such tests as may be necessary.

C6.12 The compatibility of the packaging with the user's requirements at the point of use, for example aseptic opening, should be verified by consultation with the user. Testing is rarely required.

C6.13 The sensitivity of the pack contents to particular risks, such as irradiation, moisture, mechanical shock, static discharge and the compatibility of the packaging with the contents, for example the medical device or medicinal substance, in other words, that the packaging has no adverse effect on the medical device or vice versa, will usually be apparent from historical data. When new products are to be packaged and sterilized, the instructions which the device manufacturer is required to provide should be followed.

C6.14 The protection provided by the packaging against adverse environmental influences which may reasonably be anticipated, such as mechanical shock, vibration, chemical or microbial contamination, may be considered in two stages:

a. First, the extent to which the environment to be encountered during transport and storage may be controlled. Secondly, the protection provided by the packaging.

b. Adequate performance of the packaging should be demonstrated under the anticipated conditions of use by simulating the abuses a pack may encounter during routine methods of transit and storage.

C6.15 Guidance on the methods to be adopted is given in BS 6082: 'Guide to compilation of performance test schedule for complete, filled transport packages' Part 1 'General principles' and BS 4826: 'Testing of complete filled transport packages' Parts 1-14.

C6.16 The protection provided by the packaging against microbial contamination should also be evaluated.

C6.17 Tests for bacterial penetration of packaging are beyond the experience and competence of most hospital users and could only be carried out by specialist subcontractors. There is no agreement on suitable test methods, or performance standards, for the microbial barrier properties of sterile packs.

C6.18 The microbial barrier properties of a sterile pack are dependent on both the materials of which the packaging is made and the construction of the package.

C6.19 Materials that are impermeable to gases may reasonably be assumed to present an absolute barrier to microbial contamination. When such materials are used in the construction of a pack which is hermetically sealed (for example glass ampoules) the barrier may also be assumed to be absolute.

C6.20 Package testing may be avoided by the compilation of evidence that the materials of construction are themselves an adequate barrier together with evidence that all seals and closures are adequate barriers.

C6.21 Two different approaches have been adopted to testing porous materials for their ability to exclude microbial contamination; tests based on physical particulate retention (for example the methylene blue test specified in British Standards for sterilization packaging) and tests based on the use of micro-organisms (for example the tests specified in German standards for sterilization packaging).

C6.22 For many materials a standard specification has been adopted which specifies the physical and/or chemical characteristics of the material which have been shown to provide satisfactory performance against a standard penetration test. Whenever possible materials in compliance with one of these standards should be adopted so that purchases are to an agreed specification which will give the required level of assurance.

C6.23 The methods available for verification of the adequacy of the seal or closure depend on the method chosen. Seals formed in impermeable packaging materials can be tested by one of several leak test methods but these are not generally applicable to seals formed in porous materials, nor to closures which rely upon a tortuous path to exclude microbial contamination.

C6.24 Heat seals are also dependent for their success on the performance of the heat sealer used. Several methods for testing heat seals are available but visual examination of the quality and uniformity of the seal from samples of packaging taken before and after sterilization and before and after storage and journey trials may be sufficient.

C6.25 Closures which rely on a tortuous path formed by folding are very dependent for their success on the skill of the operator forming the closure. There is good published evidence, from a number of studies carried out over many years, that the closures described in paragraphs C4.78 to C4.97 are satisfactory.

C6.26 For packaging materials to be used in gas or irradiation sterilization processes it may be necessary to determine the extent and nature of microbial contamination on the packaging before sterilization. This should not be necessary for steam sterilization processes operating at 134°C for not less than three minutes.

C6.27 When knowledge of the packaging bioburden is required this information should be sought from the packaging manufacturer or it should be determined in accordance with EN 11174 by an appropriately experienced laboratory.

C6.28 When re-usable packaging systems are being evaluated it is important that the cleaning, inspection and maintenance procedures and methods are also evaluated for their ability to consistently restore the packaging system to the required condition for re-use.

C6.29 Before any performance testing is undertaken a test protocol should be prepared. This should document:

- the tests to be performed, including full details of the equipment and methods to be used, personnel etc;
- the purpose of the tests;
- the sequence in which the tests are to be carried out;
- the format in which the results are to be documented;
- the pass fail criteria for each attribute being evaluated.

C6.30 The test protocol and the written report of the results should form part of the validation documentation.

C7. Facilities and environmental control for packaging operations

Packaging operations

C7.1 In SSDs the assembly of components, placing them in primary packaging and sealing or closing the packaging usually is referred to as a "packaging operation". Thus is in contrast to pharmaceutical and laboratory practice where the same operation is described usually as a "filling operation" and the term "packaging operation" is reserved for the subsequent, often post-sterilization, application of secondary packaging. In the following section "packaging operation" refers to the application of primary packaging and any secondary packaging which is included in the sterilization process.

C7.2 Detailed guidance on suitable facilities is given in Scottish Hospital Planning Note13; *Sterile services department* and Scottish Hospital Planning Note 29; *Accommodation for pharmaceutical services*.

General requirements

C7.3 All areas used for the reception, inspection, storage, filling, and sealing of packaging require a high standard of finish and cleanliness.

C7.4 Areas where clean, unpacked product is to be handled for, say, assembly and packaging, need a controlled environment to minimise the potential for recontamination of product by, for example mechanical ventilation or gowning procedures.

C7.5 All exposed surfaces should be smooth, water resistant and sufficiently durable to withstand frequent cleaning. The construction and any fitments should be designed to be free from crevices and sharp internal corners, which can trap dirt.

C7.6 Areas where product, ready for incorporation into primary packaging, and primary packaging materials are exposed to the environment for significant periods should be controlled to defined standards of environmental cleanliness.

C7.7 For SSDs there should be a dedicated room where the production of packs, trays etc. takes place. This should be a controlled environment. SHPN 13 recommends that packaging facilities for SSDs should be controlled to BS 5295 Class L and a detailed summary of the environmental needs of the various areas is provided in SHPN 13, Appendix 5.

C7.8 The GMP Guide for Pharmaceuticals recommends that parenteral solutions should be filled under a laminar flow work station (Grade A) within a cleanroom controlled to Grade C.

C7.9 The provision of controlled, clean environments has additional implications for staff hygiene, gowning and entry procedures and the behaviour of personnel within the facility. These requirements are fully described in the relevant GMP guides.

C7.10 Doorways throughout the facility should be wide enough, and free from damaged or rough edges, to eliminate the danger of packs of product on trolleys being damaged as they are wheeled through.

Facilities for packaging operations

Cleaning

C7.11 All operational areas of a sterile-product manufacturing facility need to be maintained to a high standard of cleanliness.

C7.12 Detailed cleaning procedures and schedules should be documented and their implementation monitored.

C7.13 For guidance on suitable procedures and schedules see ISSM Guide to Good Manufacturing Practice for NHS Sterile Services Departments and The DoH MRS Guide to Water and Environmental Cleaning.

C7.14 Surface finishes and cleaning methods must be compatible. Appendix 6 of SHPN 13 suggests appropriate finishes.

C7.15 Cleaning equipment and facilities for the storage and preparation of cleaning materials and equipment should be provided separately for areas between which cross-contamination could be problematic.

Cleaners' room

C7.16 SHPN 13 recommends the provision of a dedicated cleaning facility for the packing room, and a separate, dedicated, cleaning facility for the linen preparation area (if one is used).

C7.17 The cleaning facility provides storage for cleaning equipment and materials, a sink or sluice with hot and cold water of the appropriate quality and other facilities needed for the cleaning and preparation of the cleaning equipment. In addition, it usually accommodates consumable items for operational areas which are normally replaced by the cleaner. This would include plastic waste bags, liquid or leaf soap refills for dispensers in changing rooms etc.

C7.18 Hand washing and drying facilities should also be available in the cleaning facility.

C7.19 Whether or not separate facilities are provided, it is necessary to ensure that separate cleaning equipment is used for the assembly/packing area and other areas within the unit.

Sterile services departments - SSD

C7.20 The packing room receives single-use materials from materials' store and reusable goods after the completion of appropriate decontamination procedures.

C7.21 The decontaminated re-usable goods will include components to be incorporated into packs and may include re-usable packaging, such as textiles, instrument trays, re-usable containers.

C7.22 Within each of the areas supplying the packing room, or at the interface between these areas and the packing room there is usually provision of inspection/verification facilities to ensure that all product transferred into the packing room is the correct item and in a suitable condition for use.

C7.23 In the packing room these goods are then assembled into the combinations specified to form the pre-set trays and procedure packs which are required. These are then packed in preparation for sterilization (see SHPN 13).

Linen room

C7.24 Cleaning facility - dedicated required same as packing room. Textiles for incorporation into packs may be product items, such as surgical drapes, towels or gowns, or they may be wrapping materials.

C7.25 Textiles for wrapping purposes may be received in the SSD as laundered linen which has already been checked and folded to an agreed pattern or in bulk form, unchecked and unfolded.

C7.26 The SSD has an obligation to ensure that the laundry process is defined and controlled and the quality checks on the textiles to be used are rigorously applied to ensure that the pre-determined standard is maintained, even if the laundry has the devolved responsibility for inspecting the packaging textiles (see paragraphs C4.136 to C4.141).

C7.27 When unchecked linen is provided from the laundry, the SSD will require suitable inspection facilities within a linen preparation room.

C7.28 When textiles are to be used as the primary wrap for sterile packs they have to be inspected to a defined standard, which should include freedom from all tears, cuts and visible holes. A light table is essential for inspection to this standard.

C7.29 When the textiles are used only as an inner wrap and it is intended that the necessary bacterial barrier properties will be provided by an outer wrap of another material, such as a sterilization grade paper wrap or bag, a less rigorous inspection standard may be accepted for the textiles. A large flat surface where the wrap can be fully unfolded and a good standard of ambient lighting are still necessary.

C7.30 The linting of fabrics can be a major problem. Lint is a respiratory hazard and a fire or explosion hazard and together with other dust may contribute to an insanitary environment by providing a vehicle for the transfer of micro-organisms.

Packing room

C7.31 The activities undertaken in the packing area may be summarised as to:

- receive QC released single use, re-usable and consumable items. Note that in some units the QC inspection on cleaned and decontaminated items is carried out within the packing area. When this system is used, and particularly when inspection is done at the same time as assembly, great care is needed to ensure proper segregation of rejected items;
- assemble items into pre-set trays and procedure packs;
- verify that the contents match the specification;
- pack;
- close and/or seal the packaging system;
- label;
- verify the accuracy of the label;
- transfer to sterilizer.

C7.32 The packing room should be mechanically ventilated to ensure that the particulate count and pressure differentials meet the requirements of BS 5295 Class L in the “unmanned condition”.

C7.33 Although it may be possible to demonstrate that areas lacking mechanical ventilation can meet the required particulate standard when tested, this is not a satisfactory substitute. Mechanical ventilation is required to ensure that the particulate standard can be met consistently and also to ensure that there is a positive pressure relative to surrounding areas to minimise the ingress of contamination.

C7.34 SHPN 13 recommends that the air supply filters should have a minimum resistance of 85% when tested in accordance with BS 6540 Part 1 (EU6).

C7.35 Humidification may also be required to avoid dehydration and subsequent problems.

C7.36 When plastic materials are being used for packaging excessively dry atmospheres can promote a build up of static electricity which causes problems, such as attraction of particulate material.

C7.37 Dry atmospheres may lead also to excessively dry absorbent materials, such as paper or cotton textiles. When steam sterilized the exothermal rehydration of these materials can lead to local superheating and impairment of the sterilization process.

C7.38 Ethylene oxide sterilization requires goods to be sterilized which have been humidified to provide an optimum moisture content. This can be greatly facilitated by the maintenance of appropriate ambient humidity during assembly and packaging.

C7.39 The layout of the packing room should allow an orderly flow of work and should provide sufficient separation between activities to preclude the possibility of mix-ups, mis-labelling etc.

C7.40 Work surfaces should be of sufficient size to allow the largest wrapping materials which will be used to be fully opened without draping over the edges of the work surface.

C7.41 In-line labelling and label printing may be used to advantage, but printers are often noisy. Their location should be considered carefully to minimise the adverse effect of this noise. In addition, when it is necessary for staff to read information displayed on VDU screens it is essential that the ambient lighting is suitable.

Sterilizer loading area

C7.42 When single-ended sterilizers are used it is important to ensure adequate segregation of unprocessed goods from processed goods. Chemical process indicators in conformity to EN 867-2 may be of value.

C7.43 Adequate space must be available for the number and type of trolleys to be used.

Post-sterilization area

C7.44 This area provides the interface between the sterilizers and the processed goods store and should provide adequate space and facilities to allow product removed from the sterilizer to be inspected and to be quarantined until verification that the cycle was satisfactory.

C7.45 The area should provide space where packs may be allowed to cool to room temperature before they are handled.

C7.46 Each pack should then be inspected to verify that the packaging is not wet or damaged and that the seal or closure is intact.

C7.47 For gas sterilization processes an additional facility to provide the controlled removal of residual sterilant gas may be required. After verification that the sterilization cycle was satisfactory and inspection of the sterilized packs they may be transferred to the processed goods store or sent directly to despatch for immediate distribution.

Processed goods store

C7.48 The area should provide facilities where sterile packs may be stored away from excessively humid, hot or cold locations, strong light sources and electrical power supplies. Adverse conditions can cause deterioration of plastics, rubber and cellulosic materials found in the packaging or the contents, giving rise to embrittlement, loss of tensile strength, and so on (see SIB(7)3 ‘Storage of sterile medical devices and surgical products’, DHSS 1982).

C7.49 The storage area needs to be clean, dry and well ventilated but free from draughts. Ideally the environment in the store should be maintained at 18-22°C with RH 35-75%.

C7.50 Storage may be on open shelves or in closed cupboards. When shelves are used they may be solid or of wire mesh construction. The lowest shelf should be solid and should be 25-30 cm above floor level. The top of shelving stack should be a solid shelf 25-30 cm below ceiling level to allow room for cleaning, but should not be used for storage.

C7.51 Shelves should be located away from outside walls which can suffer from condensation problems, and from other sources of water such as sinks, and sprinklers.

C7.52 There should be no unlagged cold water pipes or other similar services which may cause condensation to form and drip onto packs.

C7.53 A high standard of cleanliness is required in this area. When facilities are less than ideal the inadequate conditions may be ameliorated by wrapping the sterile packs in a protective dust cover such as a polythene bag during storage. This may then be removed immediately prior to despatch. Note that, if packs are to be wrapped in dust covers, they must be allowed to cool to room temperature first.

Materials storage

C7.54 SHPN 13 Appendix 4 provides guidance on determining the space required.

C7.55 A materials store is required for the storage of incoming supplies, including single use items, consumables, and new re-usable items as well as packaging materials.

C7.56 The same store may also be used for incoming supplies of commercially produced supplies items (for example commercially produced sterile packs).

C7.57 The passageway between shelves or racking should be wide enough to permit proper use of handling equipment without causing damage to stored materials.

C7.58 Secure separate storage needs to be provided for the segregation of defective or non-conforming materials products.

C7.59 Facilities are required for the reception of purchased goods and subsequent inspection and confirmation that they are supplied in accordance with the purchase specification.

Packaging equipment

Heat sealers

C7.60 Several patterns of heat sealer are in common use:

a. Hand-operated heat sealers with scissor action jaws; many of these were designed for sealing light gauge polythene bags for food use and are rarely satisfactory for sterilization packaging.

b. Parallel-jaw sealers, which may be hand or foot operated, have one of the jaws heated and this presses against the opposing unheated jaw. Heat-seal packaging placed between the jaws is heated and compressed.

c. Heat-seal conveyors work in a similar manner, items to be sealed are but moved between heated elements of the conveyor.

C7.61 The seal integrity and strength is affected by the temperature, pressure and dwell time of the heat-sealing equipment.

C7.62 In order to ensure reproducible satisfactory sealing all three variables should be validated, controlled and monitored.

C7.63 Many of these heat sealers are available without a built-in timer, with no reproducible control over sealing pressure and with no indication of the operating temperature. The design of many heat sealers makes effective monitoring, calibration and adjustment of the operating conditions difficult.

C7.64 Any heat sealer which is to be used for sealing packs for sterilization should be monitored regularly for the controlling variable of temperature, pressure and dwell time. Machines which cannot be independently tested should not be used.

Overseal crimpers

C7.65 Crimping devices for the application of crimp-on overseals may be manual or automatic.

C7.66 The manual crimpers are available as hand-held devices or as bench-mounted, lever-operated machines.

C7.67 Most, if not all, of the manually operated crimping equipment available is pre-set for overseals of a particular size, or has sets of change parts to accommodate other sizes. The compressive force applied is not adjustable.

C7.68 It is essential that the crimper is only used with overseals, stoppers and containers of the pattern for which it is intended.

C7.69 Crimpers for applying foil caps to aluminium tubes for use in hot air sterilizers are also available. These are usually hydraulically operated.

Screw cappers – controlled torque

C7.70 Capping machines with a built-in, adjustable, torque limiter are available. The torque setting to be used varies with the size and type of cap and the stopper or other seal being used. The settings recommended by the manufacturer of the closure should be used.

C7.71 The calibration of the torque limiting device should be verified at regular intervals.

Ampoule sealers

Manual sealing

C7.72 Although it is possible to effectively seal an ampoule without a purpose-built ampoule sealer, it is difficult to get the correct temperature, sufficiently localised and in the required time.

C7.73 Commercially available ampoule sealers use a natural gas/compressed air (low pressure of the order of 2-3 psig) or gas/oxygen flame, in burners set either side of the ampoule.

C7.74 The ampoule stands on a support platform which is vertically adjustable to position the flames at the required position on the ampoule.

C7.75 The flames are positioned and adjusted so that the glass wall of ampoule neck is just by the points of the blue cones within the flames.

C7.76 The filled ampoule is rotated in the flame.

C7.77 When the glass in the heated region of the neck melts and starts to fuse the top of the ampoule is grasped with pliers or forceps and pulled upwards in a smooth but fairly rapid movement.

C7.78 This detaches the unwanted portion of the neck leaving a fused end which should be smooth and round without any sharp pointed protrusion or a long tail of glass.

C7.79 To produce consistently successful seals requires some skill, which is only achieved through practice and experience.

C7.80 Semi-automatic and automatic ampoule sealers reproduce the same sequence of events but the whole process is automatic.

C7.81 The flame temperature, the position of the flame, the dwell time, and the timing and rate of detachment of the neck extremity all affect the quality of the seal.

C8. Packaging operations

Routine operation, control and monitoring

C8.1 The materials, systems, equipment and procedures used should have been evaluated for their suitability before implementation for routine use (see Chapter C6).

C8.2 The following guidance is based on the assumption that high-speed packaging machinery capable of handling large batches will not be used. When large batches are to be processed on such equipment the guidance and requirements in the Regulations and Standards applicable to commercial manufacturers should be adopted.

Documentation

C8.3 There should be written specifications for all packs giving details of both the contents and the packaging requirements.

C8.4 The order in which the contents of composite packs should be placed, to facilitate their aseptic removal from the pack, should be documented in the pack specification and the associated packing procedure.

Packaging instructions

C8.5 There should be formally authorised packaging instructions for each product, pack size and type. These should normally include or make reference to the following:

a. the name of the product;

b. either a description of its pharmaceutical form and strength, where applicable, or a list of the contents of the pack;

c. the pack size expressed as the weight or volume of the product in the final container, where applicable;

d. complete list of all the packaging materials required including quantities, sizes and types, with the code or reference number relating to the specifications of each packaging material;

e. where appropriate, an example or reproduction of the relevant printed packaging materials, and specimens indicating where to apply any batch number, references and shelf life of the product;

f. any special precautions to be observed, including the order in which components should be assembled to facilitate aseptic removal;

g. a description of the packaging operation, including any significant subsidiary operations, and equipment, to be used;

h. details of in-process controls with instructions for sampling and acceptance limits, where applicable.

Batch packaging records

C8.6 When products are prepared in batches a batch packaging record should be kept for each batch or part batch processed.

C8.7 The record should carry the batch number and the quantity of bulk product to be packed as well as the batch number and the planned quantity of finished product that will be obtained.

C8.8 Before any batch packaging operation begins, there should be recorded checks that the equipment and work station are clear of previous products documents or materials not required for the planned packaging operations and that the equipment is clean and suitable for use.

C8.9 The information should be entered at the time each action is taken and, after completion, the record should be dated and signed.

Packaging records for single packs

C8.10 The records kept should have a sequential batch code enabling finished pack to the manufacturing's lot number for any single, including packaging, used in the composition of the pack.

Batch numbering

C8.11 All packs produced should have a sequential batch code enabling traceability and, when necessary, the recall of defective product.

C8.12 The batch code used should indicate the date of sterilization, the machine used and the process log/cycle number.

C8.13 Batch numbering with sterilizer and cycle may conveniently be done after sterilization when inspecting each pack to ensure that it has not become wet or sustained any damage.

Labelling

C8.14 Each sterile pack should be clearly labelled with a description of the pack contents and the description "sterile".

C8.15 Normally filling and sealing should be followed as quickly as possible by labelling to ensure that no mix-ups or mislabelling can occur.

C8.16 The correct performance of any printing operation (for example, code numbers, expiry dates), whether done separately or in the course of the packaging operation, should be checked and recorded.

C8.17 The accuracy of labelling should be checked. Special care should be taken when using individual pre-printed labels and when over-printing is carried out off-line. Roll feed labels are normally preferable to cut labels, in helping to avoid mix-ups.

C8.18 When large batches of single product are being processed the correct number of bags may be labelled for each batch. On completion of the packaging operation for each batch the number of labelled bags should be reconciled with the number of products packed and any surplus bags destroyed before commencement of a different product. Any pre-stamping or labelling of bags should be controlled by documented procedures.

C8.19 Checks should be made to ensure that any electronic code readers, label counters or similar devices are operating correctly.

Control of the packaging operation

C8.20 When setting up a programme for the packaging operations particular attention should be given to minimising the risk of cross-contamination, mix-ups, substitutions, or mis-labelling.

C8.21 Before packaging operations begin, steps should be taken to ensure that the work area and packaging equipment are clean and free from any products, materials or documents previously used, if these are not required for the current operation.

C8.22 All products and packaging materials to be used should be checked on delivery to the packaging department for quantity, identity and conformity with the packaging instructions.

C8.23 Containers and packaging for filling should be clean before filling; particular attention should be given to avoiding and removing any contaminants such as glass fragments and metal particles.

C8.24 Control of the product during packaging should include at least checking the following:

- general appearance of the packages;
- whether the packages are complete;
- whether the correct products and packaging materials are used;
- whether the labelling, including any over-printing, is correct;
- the correct functioning of packaging equipment, for example the temperature gauge reading on heat sealing equipment.

C8.25 All wrapping material used should be inspected for flaws, holes, tears, dirt, stains and other defects at the time of packaging by the operator using it.

C8.26 Any of these defects should be cause for rejection of the material, which should be scrapped.

Heat-sealing equipment

C8.27 Closing and sealing machines must be in good condition, properly set and maintained to the manufacturer's specification, and closing and sealing operations should be under constant supervision.

C8.28 For heat-sealing operations the critical variables of temperature, temperature uniformity, pressure, pressure uniformity, dwell time, and the characteristics of the packaging materials, for example the type, thickness and uniformity of the heat-seal adhesive, should, ideally, be verified at frequent regular intervals.

C8.29 If the available equipment does not provide the facility for routine monitoring of the physical operating variables then routine monitoring of process efficacy by checking the quality of the output should be adopted.

C8.30 The efficacy of the seals should be tested and proved on a regular basis, not less than daily for each heat sealer.

C8.31 As a minimum daily heat-sealing records should be kept and these should be reviewed quarterly; there should also be a quarterly check on the temperature control of each heat sealer.

Glass containers

C8.32 Because of the hazards associated with glass contamination it is essential that, if packing in glass takes place, suitable precautions are described in formal documented procedures to deal with any glass breakages which may occur.

C8.33 Equipment for handling and processing glass containers should be adequately screened to ensure that any broken glass is contained. In particular, cleaning and filling equipment must be suitably screened and it is good practice to fully enclose all conveyors between cleaning and closing.

C8.34 Conveyors for glass should not pass over areas where exposed product or components may be held.

C8.35 Suitable lidded containers to be used only for the disposal of broken glass should be provided.

QC tests

C8.36 Quantitative testing of the adequacy of packaging seals and closures requires the use of laboratory facilities and equipment not available in most hospitals.

C8.37 However, there are qualitative procedures that can be carried out which are sufficient to demonstrate a satisfactory seal, although they may be of less value in any investigation as to the cause of an unsatisfactory seal.

C8.38 These procedures are based on visual examination which can be carried out either by the operator during the various stages of the packing operation or by a QC inspector given that specific task.

Pinholes

C8.39 The performance of both porous and impermeable materials as a bacterial barrier depends on them being free from pinholes and other similar defects.

C8.40 Laboratory tests for pinholes are based on detecting the passage of a dye solution.

C8.41 However, visual examination of opaque or translucent material against a bright light is a sensitive method of detection, which may be applied in the packing room.

C8.42 The method is unsatisfactory for transparent film. However the plastic film used in pouch and reel material is typically a laminate of two films. There is a very low probability of a pinhole occurring in the same spot in both films.

Inspection of seals

C8.43 A subjective assessment may be carried out by examining and opening a number of sample packs taken from production.

C8.44 Where one of the webs being sealed is transparent the uniformity of the seal can be examined without opening the pack. In other cases it will be necessary to peel open the seal.

C8.45 In carrying out the examination the following factors should be considered:

- the appearance of the seal; it should be uniform across the entire sealed surface and should be free from creases, striations or unsealed areas;
- the seal strength; the seal should be peeled apart and attention paid to whether the force required remains constant or whether there are apparent weak spots; with practice and experience it is also possible to recognise overall increased or decreased seal strength;
- the seal characteristics; when the seal is peeled apart there should be visible evidence of the seal on both of the webs, but there should be no spitting, tearing, delamination or fibre shedding;
- the condition of the packaging, particularly in the area of the seal; excessive pressure during heat sealing may cause damage or distortion; high temperatures or prolonged dwell times may cause scorching of the paper web.

Packaging for sterile medicinal products

C8.46 Filled containers of parenteral products should be inspected individually. When inspection is done visually this should be done under suitable and controlled conditions of illumination and background.

C8.47 Operators doing the inspection should pass regular eye-sight checks, with spectacles if worn, and be allowed frequent breaks from inspection.

C8.48 When other methods of inspection are used the process should be validated and the performance of the equipment checked at intervals.

Process indicators

C8.49 A system to differentiate between processed and unprocessed items should be used.

C8.50 Single-use packaging materials may be obtained pre-printed process indicators suitable for one or more sterilization processes.

C8.51 For other packaging materials suitable process indicators may be purchased printed onto adhesive packaging tape, adhesive patches or onto labels.

C8.52 Whichever system is chosen the process indicator should conform to the requirements of the relevant European standards (BS EN 867-l and BS EN 867-2).

Sterile product release

C8.53 Post-sterilization it is necessary to verify that the sterilization cycle was satisfactory and check that each pack is either:

- labelled with a reference to the number of the sterilizer cycle through which it was processed, or
- reconciled with the load manifest for the cycle, for packs which were labelled before sterilization with a reference intended to be traceable to the cycle number.

C8.54 Packaged sterile product should be inspected after sterilization and before release to ensure that the seal or closure remains intact, and that the pack is undamaged.

C8.55 The nature of the inspection will depend upon the nature of the packaging system used.

C8.56 For example, glass ampoules may be inspected for cracks and flaws visually, by means of a dye penetration test or by means of a corona discharge crack detector.

C8.57 Whenever the integrity of the packaging is in doubt the sterilized product, or in extreme cases the sterilizer load, should be regarded as non-sterile and not released for distribution.

Operator training

C8.58 All operators should receive training in the documented procedures that they will be expected to carry out.

C8.59 Particular emphasis should be placed on operator dependent techniques such as the correct folding and closure of wraps.

C8.60 Training should include instruction on the correct use of equipment, inspection techniques and test methods and on the intended use of the product.

C8.61 Training should be documented and recorded and should be reviewed periodically.

C9. Storage and distribution

Shelf life

C9.1 Time-related expiry dates for the maintenance of sterility are widely recognised as being of little value since under artificially created worst-case storage conditions packs such as textile wrapped packs could be shown to have become contaminated within 18-30 days.

C9.2 When the products were overwrapped with a dust sheet this was extended to at least nine months, and in paper/plastic pouches was found to be at least a year.

C9.3 Maintenance of sterility depends to a great extent on the storage conditions including such factors as:

- the microbial contamination of the storage environment;
- movements of air;
- movements and behavioural standard of personnel;
- environmental temperature, relative humidity;
- moisture, such as condensation;
- location in the store, etc.

C9.4 The barrier properties of the packaging material are also a contributory factor. The general concept is that the combination of the packaging and the control exerted over storage and distribution conditions should guarantee that the contents remain sterile until opened for use.

C9.5 Some form of date coding may still form a convenient inventory control system, means of assessing the frequency of usage and for deciding whether unused packs are of a type which no longer need to be produced.

C9.6 The use of arbitrary expiry dating on packs should be replaced with batch numbering and/or manufacturing date codes which can be used to facilitate good stock rotation, based on a first-in-first-out system.

C9.7 Maintenance of sterility cannot be guaranteed once the packaging has been breached and the labelling should warn the user to verify the condition of the packaging before opening the pack for use. A warning such as “sterile unless packaging opened or damaged” is usually sufficient.

Distribution of sterilized supplies

C9.8 Trolleys used for distribution within the hospital should be covered or closed with a solid bottom shelf.

C9.9 Each article to be loaded onto a trolley or into a transit container should be inspected and handled with care; packs should not be crushed together. Cramming additional packs into too small a space will invariably result in damage.

Storage of sterile supplies

C9.10 The function of this storage area may be limited to the storage of packs produced in the SSD or may also accommodate commercially produced packs and sterile devices purchased from commercial suppliers.

C9.11 Medical equipment that has been decontaminated, disinfected, cleaned, serviced, repaired and ready for re-issue may also be stored here.

C9.12 Sufficient space is required for loading trolleys and containers distribution on site and for loading containers for delivery off site.

C9.13 Entry to the area should be restricted to authorised and trained personnel.

C9.14 Staff should wash their hands before entering; where no convenient washing facility is available, it may be acceptable to substitute treating clean hands with an alcohol-based hand rub for washing.

C9.15 Movement of personnel within the area should be kept to the minimum necessary.

C9.16 The floor should be cleaned regularly by damp mopping and/or vacuuming; sweeping, brushing or the use of rotary scrubbing and polishing machines should be avoided since these may disperse contamination from the floor as an aerosol.

C9.17 Shelves, trolleys, delivery carts and transit containers should be subject to regular cleaning in accordance with a documented procedure and schedule.

C9.18 Packs should be spaced on shelves with sufficient room to avoid friction or the jarring of adjacent products when one is removed.

C9.19 Rigid re-usable transit containers may be used with advantage to contain smaller packs; these containers should also be on the cleaning schedule.

C9.20 Packs dropped on the floor should be discarded or sent for re-processing, as applicable, unless they were protected by an outer dust cover, such as a polythene bag, show no visible damage to the packaging and do not contain items which could be damaged by impact.

C9.21 Storage arrangements should be orderly to facilitate efficient rotation of stocks, batch differentiation and ease of cleaning.

C9.22 Sterilized packs should be issued in rotation based on the First-In–First-Out (FIFO) principle in accordance with a documented procedure.

C9.23 Sterilized packs should be handled as little as possible.

C9.24 After sterilization it is important that packs are stored safely in a manner which will assist in preserving the sterility of the contents.

Handling sterile packs

C9.25 It is important that all personnel who will be required to handle sterile packs (porters, drivers, SSD assistants, phlebotomists, nurses, clinicians, etc.) receive appropriate training in the correct handling procedures and why they are necessary.

C9.26 Many sterile packs will contain expensive and delicate instruments and require careful handling. All sterile packs need to be handled in a manner which will not compromise their sterile condition.

C9.27 As a minimum the following rules should apply:

a. The hands of personnel who will handle sterile packs need to be clean and dry;

b. The sterile packs need to be kept dry and must not be torn, punctured or otherwise damaged;

c. Any packs that are visibly damaged, stained or wet should be returned to the SSD for disposal or re-processing, as appropriate;

d. It should be possible to verify that the pack has been processed; this may be by means of a process indicator, or by appropriate labelling such as a sterilizer cycle number. Note that process indicators do not indicate the sterility of the pack contents, only that the pack was processed through a sterilizer;

e. Containers, distribution trolleys and any surfaces on which the packs will be placed must be clean and dry.

Transport and distribution

C9.28 There should be documented procedures for delivery and for the packaging, collection and return of used goods.

C9.29 Containers and trolleys should be easy to clean, properly maintained and should adequately isolate the goods in transit from environmental hazards.

C9.30 The cleaning procedure for bulk containers and trolleys should be documented and records should be kept of cleaning carried out.

C9.31 In transit the contents of containers should be adequately identified by means, such as labels, which will not be erased in transit.

C9.32 Used goods being returned must be segregated from clean and sterile goods being delivered.

C9.33 Vehicles reserved for the delivery of clean and sterile goods should be used whenever possible. If dedicated vehicles are not used then each vehicle used must be cleaned after use for the return of used goods and before use for the transport of sterile goods.

C9.34 The cleaning procedure for the vehicle interior should be documented and records should be kept of cleaning carried out.

C9.35 As an alternative the use of sealed leakproof containers may be used for transport in either or both directions.

Storage in clinical areas

C9.36 The same principles apply as were discussed for the processed goods store.

C9.37 The storage facility should be secure, easy to clean and organised to aid stock rotation (for example a double-sided cupboard filled from the back but where goods are removed from the front).

C9.38 The quantity of goods stored should be limited to those actually needed within a reasonable time period.

C9.39 The place and method of storage varies, but it should be separate accommodation, not a general store with bedpans, urinals etc.

C9.40 Storage should be segregated or, if it has to be shared, it should be with other clean and/or sterile equipment.

C9.41 A high standard of cleanliness is required and packs must be kept well away from sinks and other sites of possible contamination.

Packaging for return of used items for re-processing

C9.42 A local policy for the handling of potentially contaminated and hazardous items, and practices for safe containment during transport back to the SSD need to be established.

C9.43 All returned items should be regarded as potentially contaminated and thus infective.

C9.44 Containers for returning goods should be leak proof, securely closeable and safe to handle. The container design should include the facility for clear labelling to indicate the nature of the contents.

Glossary of terms

Bioburden	Population of viable micro-organisms on an item.
Capacity (for glass containers)	The internal volume at 20°C.
Closure	Means used to close a package where no seal is formed, for example by repeated folding to construct a tortuous path.
Closure integrity	The quality of the closure which ensures that it presents a microbial barrier.
Final pack	The pack in which a medical device is sterilized. In addition to the primary pack a secondary and/or transport pack may be included.
Internal pressure resistance	The internal hydraulic pressure which a glass container at 20°C can withstand without breaking.
Microbial barrier	The ability to prevent the ingress of micro-organisms.
Multi-trip container	A glass container which has strength characteristics sufficient for it to withstand a number of filling/use operations.
Packaging compatibility	The ability of the packaging material and/or system to achieve the required performance without detrimental effect on the medical device.
Packaging material	Any material used in the fabrication or sealing of a packaging system or primary pack.
Packaging system	One or more packaging materials assembled into a single unit intended as part or all of a primary pack.

Primary pack	The sealed or closed packaging system forming a microbial barrier enclosing the medical device, and (usually) in contact with the medical device.
Seal	The result of joining of layers, for example by use of adhesives or thermal fusion.
Seal integrity	The quality of the seal which ensures that it presents a microbial barrier.
Secondary pack	The pack containing one or more medical devices, each in its primary pack.
Shelf pack	see Secondary pack.
Shipper pack	see Transport pack.
Single-trip container	A glass container designed and manufactured to be sufficiently strong to withstand only one filling/use operation.
Terminally sterilized	Descriptor for medical devices which are sterilized after being completely sealed or enclosed in at least the primary pack.
Thermal shock resistance	The ability of a glass container to withstand a sudden temperature change without breaking.
Transport pack	The pack containing one or more primary and/or secondary packs intended to provide the necessary protection during transport and storage.
Ullage	That part of the contents of a container which wants for filling. Expressed in units of volume or as a percentage of the total container volume.
Unit pack	see Primary pack.
Vacuity	The free space left above the contents in a sealed container expressed as a percentage of the nominal volume of the contents.
Validation	Documented procedure for obtaining, recording and interpreting the data required to show that a process will comply with predetermined specifications.

SECTION D

A Contract for the Annual Testing of Sterilizers

GC/Works/4 (1998)

INVITATION TO TENDER

Works: **Annual Testing of Sterilizers**

Site: _____

1. You are invited on behalf of _____NHS Trust to tender, upon the basis of GC/Works/4 General Conditions (1998), for the Works described in the following enclosed documents:

   a. Abstract of Particulars;

   b. Supplementary Conditions and Annexes referred to in the Abstract of Particulars;

   c. Specification for the Annual Testing of Sterilizers.

2. Your tender with the completed Abstract of Particulars and Supplementary Clauses should be submitted on the Form of Tender and Tender Price Form also enclosed. Any obvious errors in pricing or errors in arithmetic will be dealt with as stated in the Form of Tender.

3. You are required to keep your tender confidential and not divulge to anyone, even approximately, what your tender price is or will be. The sole exception to this is information you may have to give to your insurance company, or broker, in order to compile your tender, but you must stress to them that this information is given in strict confidence.

4. You must not make any arrangements with anyone else about whether or not they should tender, or about their or your tender prices or terms and conditions. You may however, obtain any necessary subcontract quotations.

5. No tendering expenses will be reimbursed by the Employer.

6. Tenders received late will not be considered unless due to genuine postal delays. If the tender is qualified it may be set aside, or you may be required to withdraw the qualification without amending your offer. Any proposals for alternatives to the specified requirements should be submitted by way of a separate, unqualified, bid, after checking with the Employer on the procedure to follow.

7. The Employer does not bind himself to accept the lowest, or any tender.

8. Your form of tender should be submitted in a sealed envelope prominently marked:

   FORM OF TENDER FOR ANNUAL TESTING OF STERILIZERS

   The envelopes should bear no external indication of the identity of the tenderer.

9. Tenders must be completed and returned by 12 noon on _____

   To: _____

   SIGNED by

INDEX

Page No.

INSTRUCTIONS FOR TENDERERS

Tenders for the work included in the following Tender Document shall be written on the attached Form of Tender. The Price Schedule must be fully priced, extended and totalled throughout in black ink and returned under sealed cover to the _____

to arrive not later than Noon on _____ endorsed on the outside "Tender for the Annual Testing of Sterilizers."

Tenders to remain open for acceptance for a period of 60 days from the above date.

_____NHS Trust reserves the right to decline the lowest or any Tender and no expense in submitting a tender will be reimbursed.

Tendering procedures will be in accordance with the principles of the "Code of Procedure for Single Stage Selective Tendering 1996", the examination and correction of priced Bills of Quantities being in accordance with Alternative 2 of paragraph 6.4 of that Code.

In the event of a Contractor not tendering, the documents are to be returned immediately to the Project Manager.

The Contractor shall comply with the requirements of all regulations, codes and statutes applicable to the execution of the works.

Where in the opinion of the Project Manager any of the finished works or materials or workmanship in any part of the works, do not comply with all the relevant requirements of this specification and drawings, that part of the works shall be classified as defective work.

All work classified as defective work shall be made good to the satisfaction of the Project Manager.

TENDER AND TENDER PRICE FORM

THE ANNUAL TESTING OF STERILIZERS

_____NHS Trust

To be returned by 12 Noon on _____ to _____

1 We have examined GC/Works/4 General Conditions (1998), and the following documents:

a. Abstract of Particulars;

b. Supplementary Conditions and Annexes referred to in the Abstract of Particulars;

c. Specification for the Annual Testing of Sterilizers.

2 We have obeyed the rules about confidentiality of tenders and will continue to do so as long as they apply.

3 We submitted to the Employer a Price Schedule and Summary of prices with an alternative. We undertake to satisfy the Employer that the prices in the summary are fair.

4 We agree that, should errors in pricing or errors in arithmetic be discovered in the summary submitted by us during consideration of this offer, we will, in addition to the chance to confirm the offer as tendered despite the errors, be afforded the opportunity of withdrawing it.

5 Subject to and in accordance with paragraphs 3 to 5 above and the terms and conditions contained or referred to in the documents listed in paragraphs 1 and 2, we offer to execute the Works referred to in the said documents in consideration of payment by the Employer of the sum shown in our accompanying Tender Price Form, which shall be deemed to form part of our tender, plus reimbursement by the Employer of Value Added Tax in accordance with Condition 19 (*VAT*).

6 We agree that differences or questions arising out of or relating to the Contract shall be resolved in accordance with Condition 28 (*Adjudication*) of the General Conditions.

SIGNED by
for and on behalf of
Tel:
Fax:
Telex:
Date:

TENDER PRICE FORM

THE ANNUAL TESTING OF STERILIZERS

_____NHS Trust

To be returned by 12 Noon on _____ to _____

The sum referred to in our accompanying form of Tender is;

£_____for Year One

and/or

Alternative No. 1

£_____for Five Years.

Alternative No. 2

£_____for Five Years.

£_____% materials on cost

SIGNED by

for and on behalf of

Tel:
Fax:
Telex:
Date:

ABSTRACT OF PARTICULARS

Works : THE ANNUAL TESTING OF STERILIZERS

Site:_____NHS Trust

Condition 1(1) (*Definitions, etc.*) Employer

The Employer shall be the _____NHS Trust,

Conditions 1(1) (*Definitions, etc.*): Project Manager, and 3 (*Delegations and representatives*)

The Project Manager shall be Mr_____

_____NHS Trust

who shall act generally on behalf of the Employer in carrying out those duties described in the Contract, subject to the following excluded matters:

In relation to such excluded matters, the person authorised to act for the Employer is:

Mr _____

Only Regulations 7 and 13 of the CDM Regulations apply.

Condition 7 (*Defects in Maintenance Periods*)

Condition 7 shall apply.

The Maintenance Period for the Works shall be six months for any work done and 12 months for parts supplied and fitted and shall apply from the day after that on which the Works are completed as certified by the Project Manager.

Condition 8 (*Occupier's rules and regulations*)
The rules and regulations for _____ NHS Trust are appended.

Condition 12 (*Passes*)
Passes are required for admission to the Site.

Condition 15 (*Commencement and completion*)
Period within which Order to Proceed: within Ten Days of the acceptance of the tender.

The Date for Completion of the Works shall be _____

Condition 20 (*Advances on account*)
Condition 20 shall not apply.

Condition 26 (Damages for delay)
Damages for delay shall be at large.

Condition 28 (Adjudication)
The adjudicator shall be as agreed by the Employer and the Contractor.

Item	Preamble	£	P
	FORM TYPE AND CONDITIONS OF CONTRACT The works shall be carried out and completed in accordance with the rights and duties of GC/Works /4. The expression “the Contract Documents” shall mean, the Specification, the Price Schedule, the Tender and the letter of acceptance. The Contract shall be deemed to be a Scottish Contract and shall be construed and the rights of the parties and all matters arising hereunder determined in all respects according to the Laws of Scotland.		
	Amount to Collection Page		

Item	Preamble	£	P
	SCHEDULE OF CLAUSES 1 Definitions 1A Fair dealing 2 Contract documents 3 Delegations and representatives 4 CDM Regulations 5 Protection of Works 6 Loss or damage 7 Defects in Maintenance Period 8 Occupier's rules and regulations 9 Discrimination 10 Corruption 11 Site admittance 12 Passes 13 Photographs 14 Official Secrets and confidentiality 15 Commencement and completion 16 Extensions of time 17 Project Managers Instructions 18 Valuation of Instructions 19 VAT 20 Advances on account 21 Final Account 22 Certification 23 Withholding payment 24 Recovery of sums 25 Suspension for non-payment 26 Damages for delay 27 Determination by Employer 28 Adjudication 29 Choice of Law 30 Assignment and subletting 31 Other Works		
	Amount to Collection Page		

Item	Preamble	£	P
	SUPPLEMENTARY CLAUSES **Asbestos** If during the execution of the work, the Contractor discovers any material suspected of being asbestos, the following procedures will apply: 1. Immediately cease work in the suspected areas. 2. Immediately notify the Project Manager by telephone, then confirm same in writing. 3. Do not commence work in the area(s) involved until instructed by the Project Manager. **Noise Control** The Contractor shall comply with statutory requirements relating to control of noise levels on site, include for complying with DOE Advisory Leaflet No.72 Noise Control on Building Sites and for fitting all compressors and percussion tools with effective silencers of a type recommended by the manufacturers of the compressors or tools. The Contractor shall not use pneumatic drills or other noisy appliances outwith normal working hours without consent of the Project Manager . The Contractor shall not use or permit employees to use radios or other audio equipment. **Inspection of Work before Covering** In cases where the Project Manager has given notice to the Contractor that the work must be inspected and/or tested previous to same being covered up or hidden, the Contractor shall give adequate notice in writing to the Project Manager before any such work shall be so covered up or hidden. Should the Contractor fail to give such notice he may be required to uncover same and make good at his own expense. **Programme** The Contractor shall prepare and submit to the Project Manager within two weeks of agreement of access and site occupation with the Employer, a programme in a form as required by the Project Manager, which shall clearly set forth the sequence of all operations and the time limits within which the Contractor proposed that each operation shall be commenced and completed. The Contractor, in the preparation of this programme, shall be held to have co-ordinated the while works embraced in this Contract.		
	Amount to Collection Page		

Item	Preamble	£	P
	On agreement or negotiated amendment of the programme by the Project Manager, the Contractor shall be responsible for the execution of the works in conformity therewith. He shall submit copies of same, record progress and update or redraft as required to take account of any circumstances which arise affecting the progress of the works. **Limitations of Working Space** The Contractor shall not be allowed to use existing roadways or footpaths for parking or depositing material or plant unless he is given prior approval by the Project Manager . The Contractor shall at all times confine his workpeople to those parts of the site and building on which he is engaged and shall on no account allow them to trespass into any other parts of the site and buildings without the prior consent of the Project Manager . The contractor shall not be allowed to erect temporary buildings, deposit plant, store materials or rubbish on any part of the property or grounds outside that assigned to him for this contract. The Contractor shall allow in his tender for all necessary preparatory work and later, at the completion of the contract, for removing debris and reinstating the storage etc. areas to their original condition, all to the satisfaction of the Project Manager . The original condition shall be established with the Project Manager prior to the commencement of work. The Contractor shall take all necessary precautions to minimise nuisance or discomfort to the occupiers of adjacent premises arising from his operations. Any damage, structural or otherwise caused to the existing buildings by the construction process shall be made good at the Contractor's expense.		
	Amount to Collection Page		

Item	Preamble	£	P
	The Employer reserves the right to send their own or other workmen to the site to execute work not included in this contract and the Contractor shall be required to afford such workmen all reasonable facilities for the execution of their work but the Contractor shall not be entitled to any profit on the cost of such work. The Contractor will liaise and co-operate with the Project Manager and will take all reasonable steps to ensure that the works are carried out in such a fashion as will in no manner, or at any time, impair the security of the existing buildings. All scaffolding or temporary access will be erected in such a fashion as, without in any way impairing the stability of the scaffold, will prevent ease of access to the scaffold by any unauthorised person. The Contractor shall maintain permanent supervision and attendance at mechanical or other dangerous plant, when in use, to ensure the safety of the staff, patients and others using the hospital. Alternatively all such plant and equipment shall be kept in a secure compound to prevent unauthorised access. On no account shall any ladders or tools be left unattended and at the end of each day's work all plant shall be removed and placed in the Contractor's site hut or other secure place. No windows, doors or hatches have to be left open after workmen have left site. The Employer will not be responsible for any such acts of vandalism by any person, to the Contractor's materials or plant. All materials will be disposed of in a proper manner off site. Any skips brought to site shall have lids which shall be securely closed when not attended. The Contractor shall not use existing sanitary fittings, gullies or drains to dispose of any materials including paint, turpentine, oils, etc. The area immediately around the site must be kept clear of rubbish, protective casings and coverings and general debris at all times. No scattered or accumulated debris will be allowed to gather and the Project Manager may require daily cleaning or clearings of any such debris to ensure compliance with this requirement. **Working Hours & Access to Site** Access will normally be outside normal hours (0800-1700 Monday to Friday). No additional costs due to overtime working will be paid for by the Employer unless that overtime has been instructed in writing by the Project Manager and he will clearly state in writing that the additional cost will be borne by the Employer. Any overtime thus authorised will be based on the standard time rates and paid net.		
	Amount to Collection Page		

Item	Preamble	£	P
	Any overtime working by the Contractor must be agreed beforehand with the Project Manager and it should be noted that any additional costs of supervision on behalf of the Employer will be paid by the Contractor. **Fire Precautions** The Contractor is to take all necessary precautions to prevent loss or damage from fire. The Contractor is to familiarise himself and staff with all fire escape routes and procedures in use within the property involved. All escape routes to be kept operational during occupation by the Employer. **Existing Services** The Contractor shall not interfere with the operation of the existing services, such as gas, water, electricity, telephones, buried cables sewers and the like without permission of the Project Manager . **Smoking/Alcohol Policy** Smoking or the consumption of alcohol will not be permitted within any Employer property. **Employer Facilities and Equipment** All equipment necessary to carry out the works shall be provided by the Contractor. Employer equipment shall not be used. **Health, Safety and Welfare** The Contractor shall identify a Safety Officer responsible for all aspects of Health, Safety and Welfare on site including the control and actions of all Sub-Contractors in this respect. The Contractor shall permit access to the site by the Employers designated Safety Advisers who shall have the right to enter onto the Site at any time without prior notice to the Contractor. The Contractor shall implement any recommendations with regard to Health, Safety and Welfare measures which may be made by the Employer's designated Safety Advisers. Such recommendations shall not be deemed variations to the Contract if they are necessary, in the opinion of the Employer's designated Safety Adviser, to comply with the terms and conditions of any relevant Health, Safety and Welfare Acts or Regulations. The Contractor shall be deemed to be familiar with the Employer's document "Health and Safety Guide for Contractor's" and shall comply with its requirements as necessary. A copy of this document may be obtained from the Project Manager.		
	Amount to Collection Page		

Item	Preamble	£	P
	Joint Code of Practice on the Protection from Fire of Construction Sites and Buildings Undergoing Renovations, Fourth Edition, June 1997. The Contractor's attention is drawn to the above Joint Code published by the Building Employers Confederation. The Contractor shall allow for compliance with the recommended standards in this Code of Practice. This contract is not deemed a "Large Project". **Method Statement** The Contractor shall present Method Statements which will describe fully his operations on site and discuss and agree with the Project Manager and Planning Supervisor prior to the commencement of the Works. The method Statements shall in particular include details about:- 1. General Site Safety 2. General Site Security 3. Protection of the General Public 4. Protection of Patients, Visitors and Staff using the Premises, etc. 5. Access and Exit Arrangements **General Facilities and Obligations** Maintaining, altering, adapting and clearing away any temporary works and making good after same shall be deemed to be included with the items. Notices, rates, fees and charges to Local Authorities and public undertakings related to the following items shall be included in the appropriate items. The Contractor shall obtain all necessary Planning and other permission for all temporary accommodation. **Pricing** Plant, tools and vehicles. Scaffolding and temporary access. Site administration and security, including safeguarding the work, materials and plant against damage and theft, include for providing all watching, accommodation and lighting if necessary. Transport of work people. Protecting the works from inclement weather.		
	Amount to Collection Page		

Item	Preamble	£	P
	Lighting and Power for the Works Electrical power at 240 volts 50 cycles/single phase/AC required for the works will be provided free of charge by the Employer. *(Note: This should be suitably transformed to 110V for the use of power tools).* Temporary connections will be located and carried out in strict conformity with the Employer Authority's requirements and shall be approved by the Project Manager before work commences. The Contractor shall not use power provided for the Works, by the Employer for cooking facilities or heating. Building (Safety, Health and Welfare) Regulations and Health and Safety at Work Act in respect of all work people will apply. Removing rubbish, debris, protective casings and coverings from the site and cleaning the works internally and externally. These to be removed regularly and the site to be kept clean. On completion, the works shall be cleaned, which shall be deemed to include where necessary scrubbing floors, cleaning glass both sides, removing all stains from facework, cleaning sanitary fittings and leaving the whole premises clean and ready for occupation. The Contractor may make reasonable use of existing facilities as he so wishes subject to the approval of the Project Manager with the Employer's consent. **Insurance** Allow for the costs in complying with insurance provisions. **Materials and Workmanship** The Contractor will supply all materials that may be necessary for the due and proper completion of the work (except those materials specified to be supplied by the Employer under direct purchase arrangements or as part of sterilizer testing agreement). The materials shall be new unless otherwise described and shall be the best procurable of their respective kinds and so far as practicable. All goods and materials unless otherwise described, shall be in accordance with the latest revised BS current at the date of tendering. The contractor shall be responsible for providing all tools, equipment and instruments for the execution of the work. This is to include provision of 3 sets of Huckaback towels or cotton sheets to the requirements of SHTM 2010 Part 3. The Contractor shall provide all labour and pay all expenses in connection therewith and do everything necessary for the due and proper completion of the work. Workmanship shall be in accordance with the latest revised BS Code of Practice. **Samples** Samples of proposed materials and workmanship shall, if required by the Project Manager be submitted for approval and those samples kept by the Project Manager who shall have the power to reject all such materials and condemn such workmanship as do not correspond with the approved samples.		
	Amount to Collection Page		

Item	Preamble	£	P
	Nuisance The Contractor shall take the necessary precautions to prevent nuisance from water, smoke, dust, rubbish and other cause. **Existing Furniture, Fittings and Equipment** Prevent damage to any furniture, fittings and equipment left in the existing property. Move as necessary to enable the work to be executed, cover and protect as necessary and replace as required. Including but not limited to: Fire fighting equipment, carpets, shelving, building fabric etc. **Making Good Defects** Allow for arrangements with the Employer and giving reasonable notice of the precise dates for access to the various parts of the Works for the purpose of making good defects. **Maintenance Instructions** Where applicable allow for obtaining and handing over to the Project Manager at practicable completion any maintenance instructions provided by manufacturers, suppliers or sub-contractors. **Control of Noise, Pollution and all other Statutory Obligations** The attention of the Contractor is drawn to the provisions of Section 60 of the Control of Pollution Act 1974 with reference to the control of noise in relation to any demolition or construction works and the need, particularly where such works are adjacent to occupied property where a high sensitivity to noise may be anticipated to ascertain what requirements, if any, shall apply to the works in this respect. The restrictions may relate to the type of plant to be used, the methods of working to be adopted, the hours of working permissible and may in addition impose a maximum noise level at the site boundary which may not be exceeded. The Contractor is to be held responsible for complying with such requirements, restrictions or consents, together with any other stipulations to which his attention may be drawn from time to time by the competent Authorities and is to allow in his tender for any costs or expenses arising from such compliance. No instructions issued to the Contractor by the Project Manager or his authorised representative shall relieve the Contractor from compliance with the Control of Pollution. The Contractor will at all times ensure that his operatives create the minimum of noise consistent with the work being undertaken. All necessary noise, including the playing of transistor radios and like will be prohibited. No discomfort or annoyance from the noise will be occasioned to patients or staff where such noise is reasonably avoided.		
	Amount to Collection Page		

Item	Preamble	£	P
	Fire Precautions Before any works are carried out, the Contractor is to discuss his proposals with the Project Manager and Fire Prevention officer, to ensure that he is fully aware of any fire hazard that may be involved. He is to draw the attention of all his workmen to the special vulnerability of Employer property and patients in the event of fire, and the dangers involved in the careless disposal of matches, cigarettes and tobacco ash must be fully impressed on them. The Contractor's workmen are to be required strictly to conform with all "NO SMOKING" rules applicable in specific areas of the property. Fire escape routes are to be kept unobstructed and, if necessary illuminated at all times and the Contractor will post such notices as are necessary to ensure compliance with this requirement. **Year 2000 Compliance** Prior to the start of the project certificates of Year 2000 compliance must be made available to the Project Manager demonstrating that any parts or equipment to be installed is compliant with: BSi DISC PD 2000-1 A Definition of Year 2000 Conformity Requirements. NHS Estates Guidance, The Year 2000 problem, Testing of estates embedded systems and devices. Details of year 2000 compliance tests and test procedures must be submitted to the Project Manager for all the equipment being installed. On completion of the project, or stages of the project, Year 2000 compliance must be demonstrated and certificates issued to the Project Manager before the systems become operational.		
	Amount to Collection Page		

Item	Preamble	£	P
	COLLECTION PAGE Amount of total from Page No. 135 Amount of total from Page No. 136 Amount of total from Page No. 137 Amount of total from Page No. 138 Amount of total from Page No. 139 Amount of total from Page No. 140 Amount of total from Page No. 141 Amount of total from Page No. 142 Amount of total from Page No. 143 Amount of total from Page No. 144		
	Amount to Price Schedule Summary		

APPENDIX 1

SCHEDULE OF INFORMATION TO BE SUPPLIED BY THE TENDERER

SITE .....

SERIAL NO.	ITEM	TO BE COMPLETED BY THE TENDERER
1.	Names of Technicians allocated to the above site.	
2.	The precise details of the qualifications and experience of the above technicians.	
3.	The average number of technicians available off site for unplanned or emergency work.	

Signed ..... in capacity of .....

For and on behalf of (IN BLOCK CAPITAL)

.....

Date .....

APPENDIX 2

LIST OF SUB-CONTRACTORS

The contractor shall list hereunder the names of the Sub-Contractors he proposes to employ on the Works.

Work Section or Trade	Name/Address/Tel. and Fax No. of Sub-Contractor

Signed by…… Date…….

In Capacity of……..

For and on behalf of……..

APPENDIX 3

SCHEDULE OF CONTRACTOR'S PARTICULARS

Contract:

The Annual Testing of Sterilizers

Contractor's Title:

Address:

Day Telephone Number:

Emergency Telephone Number:

Facsimile Number:

Contractor's Representative for this Contract:

Daytime Telephone Number:

Emergency Telephone Number:

Facsimile Number:

VAT Registration Number:

Date of Expiry of Insurance Policy:

Signed by…….. Date…….

In Capacity of……..

For and on behalf of……..

EMERGENCY REPAIRS

The Contractor must state below the emergency telephone numbers at which his emergency repair staff can be contacted and called out immediately at any time to deal with emergencies occurring at the Contract Works.

Contractor to state here his emergency repair telephone numbers:

THIS SECTION MUST BE COMPLETED AT TIME OF TENDER

CERTIFICATE OF COLLUSION

_____NHS Trust

to be returned by _____

The essence of selective tendering is that the client shall receive bona fide competitive tenders from all those tendering. In recognition of this principle we certify that this is a bona fide tender, intended to be competitive and that we have not fixed or adjusted the amount of the tender by or in accordance of any agreement or arrangement with any other person. We also certify that we have not done and we undertake that we will not do at any time before the hour and date specified for the return of this tender any of the following acts:-

a. communicating to a person other than the person calling for those tenders the amount or approximate amount of the proposed tender, except where the disclosure in confidence of the approximate amount of the tender was necessary to obtain insurance premium quotation required for the preparation of the tender.

b. entering into any agreement or arrangement with any other person that he shall refrain from tendering or as to the amount of any tender submitted.

c. offering or paying or giving or agreeing to pay or give any sum of money or valuable consideration directly or indirectly to any person for doing or having done or causing or having caused to be done in relation to any other tender or proposed tender for the said work any act or thing of the sort described above.

In this certificate the word “person” includes any person and any body or association, corporate or unincorporate and “any agreement or arrangement” includes any such transaction, formal or informal, and whether legally binding or not.

Signed…….

on behalf of……

……..

Date……

PRICE SCHEDULE

SUMMARY

YEAR ONE

a. The price in this Schedule covers the cost of working within the hours as listed in the Preamble, Appendix A: Sterilizer inventory and Unit Costs.

b. Sterilizer testing shall be carried out in accordance with the advice contained in the appropriate Appendix at the frequencies stated.

c. Value Added Tax shall be reimbursed as stated in the Tender.

d. The price inserted in this Schedule shall include:

A.	**Preamble: Collection page**	**£**
B.	**Testing the cost of all visits as detailed in Appendix A of the particular specification**	**£**
C	**Compiling reports, copying and determining tests**	**£**_____
Total Cost (excluding VAT)	**To Tender Price Form**	**£**_____
Alternative No. 1.	Year No. 1 from Above	£
	Year No. 2 +……..%	£
	Year No. 3 +……..%	£
	Year No. 4 +……..%	£
	Year No. 5 +……..%	£_____
Total Cost (excluding VAT)	To Tender Price Form	£_____
Alternative No. 2:	Years 1-5 Fixed Price	£_____
Alternative No. 2	To Tender Price Form	£_____

Note:

Tenderers may price for one or both of the above options.

Materials

All material costs to include administration, ordering, delivery and handling charges.

Material invoices will accompany all claims for payment.

Material shall be charged at cost plus… _____%

Signed _____ in the capacity of _____

(IN BLOCK CAPITALS) _____

on behalf of _____

_____

Telephone No_____Date_____19_____

Summary 3

Summary of staff rates

The rates below will apply to work not covered in this contract requested for the sterilizers listed in Appendix A

The rates below are to be valid for a period of _____ years

Rates per hour			**Overtime Rates**			
Grade of staff	**Trade**	**Standard rate**	**Mon - Fri**	**Sat & Sun**	**Public Hols**	**Callout Rate**
Technician						
Supervisor						
Any other staff as appropriate						

Signed_____ in the capacity of _____

(IN BLOCK CAPITALS)_____

On behalf of _____

Telephone No _____ Date _____ 19_____

TERM CONTRACT FOR ANNUAL TESTING OF STERILIZER

INVITATION TO TENDER – SHEET 1

……..NHS TRUST / EMPLOYER
……...
……
……

Contract No ……..

FOR TRUST/ USE

You are invited by the above NHS Trust/Employer to submit on this form , which together with all documents when completed is to be delivered to the above NHS Trust Employer……. on…… 1999……. the enclosed label being

The NHS Trust Employer do not bind themselves to accept the lower or any

IF NO TENDER IS BEING SUBMITTED ALL OF THE DOCUMENTS SHOULD BE RETURNED WITHOUT DELAY USING THE ADDRESSED LABEL WHICH SHOULD BE MARKED 'NO TENDER'.

FORM OF TENDER

TO THE ……..NHS TRUST/EMPLOYER

FOR THE ANNUAL TESTING OF
(hereinafter referred to as ' the Employer

1. I/We have examined the following parts of the Contract

    1. Invitation to
    2. Price
    3. VAT Form
    4. Schedule of Information to be supplied beTendere
    5. Abstract of
    6. General Conditions of
    7. Particular

and subject and in accordance with the terms and conditions in the Contract. I/We offer to execute all the work described in the said documents during the contract period defined in the Conditions of Contract commencing……1999…….. at such times as may be set forth therin or as the Employer may otherwise order, in consideration of:

A. Payment by Employer at the rates or prices I/We have inserted in the said Schedule, as detailed in Annexe A.

B. Reimbursement by the Employer of Value Added Tax to be declared to HM Custom and Excise.

INVITATION TO TENDER – SHEET 2

2. The essence of selective tendering is that the NHS Trust/Employer receive bona fide competition tenders from all persons tendering. In recognition of this principle:

I/We certify that this is a bona fide tender, and that I/We have not fixed or adjusted the amount of the tender by or under or in accordance with any agreement or arrangement with any other person. I/We certify that I/We have not done and I/We undertake that I/We will not do at any time before the hour and date specified for the return of this tender any of the following acts:

A. communicate to a person other than the person calling for those tenders the amount or the approximate amount of the proposed tender, except where the disclosure, in confidence, of the premium quotations required for the preparation of the tender;

B. enter into any agreement or arrangement with any other person that shall refrain from tendering or as to the amount of any tender to be submitted;

C. offer or pay or give to pay or give any sum of money or valuable consideration directly or indirectly to any person for doing or having done or causing or having caused to be done in relation to any other tender or proposed tender for the said work any act or thing of the sort described.

In this invitation the work 'person' includes any person and any body or association, corporate or unincorporate; and 'any agreement or arrangement' includes any transaction, formal or informal, and whether legally binding or not.

3. I/We agree that other terms or conditions of contract or any general reservations which may be printed on any corresponding emanating from me/us in connection with this tender or any other agreement resulting from this tender, shall not be applicable to this tender or to the Agreement.

Signed……..in the capacity of……
duly authorised to sign tenders for and on behalf of

(IN BLOCK CAPITALS)……..

Telex No…….. Fax No……

Postal Address……

……

Telephone No…… Date……..199……

Contractor's nominal liaison officer:……

……..

PRICE SCHEDULE

……NHS TRUST/EMPLOYER Contact No……..

THE WORK

1. The price in this Schedule covers the cost of working within the outside normal hours as indicated in Appendix A: Sterilizer Inventory and Unit Costs.

2. Sterilizer testing shall be carried out in accordance with the advice contained in the appropriate Appendix at the frequencies stated.

3. Value Added Tax shall be reimbursed as stated in the Tender.

4. The price inserted in this Schedule shall include:

A. the cost of all visits;

B. the cost of compiling reports, copying and determining tests.

Total Cost (excluding VAT) £……

Signed……in the capacity of……..

(IN BLOCK CAPITALS)……

Telex No…… Fax No……

Postal Address……

……

Telephone No…….. Date……..19……..

VALUE ADDED TAX FORM

…… NHS TRUST/EMPLOYER

……

……

……

……

……

Job Title – Annual Testing of Sterilizers Contract No……

To: The Chairman and Members of the ……NHS Trust/Employer

I/We the undersigned, hereby give our Provisional Assessment of Value Added Tax payable on positively – rated Taxable Supplies of goods and/or Services chargeable to the ……

Description of Goods and/or Services	**Value (Tax Exclusive) £**	**Positively Rated at: %**	**Tax £**

Total £……

Signed…… Date……

On behalf of……..

Contract No……

.

SCHEDULE OF INFORMATION TO BE SUPPLIED BY THE TENDERER

SITE……

SERIAL NO.	ITEM	TO BE COMPLETED BY THE TENDERER
1.	Names of Technicians allocated to the above site.	
2.	The precise details of the qualifications and experience of the above technicians.	
3.	The number of technicians available off site for unplanned or emergency work.	
4.	The location of off site technicians who will respond to unplanned or emergency requirement.	OFFICE LOCATION 1. …… 2. …… 3. ……
5.	The location from which out of-hour call outs will be arranged.	OFFICE ADDRESS 1. …….. 2. …… 3. …….. TELE ……

Signed……in capacity of……

On behalf of (IN BLOCK CAPITAL)

……

Date……

ABSTRACT OF PARTICULARS

The following shall be read in conjunction with the General Conditions of Contract.

1. DEFINITIONS

Refer to;

1.04 The Schedule(s) shall be the Price Schedule(s) for the Annual Testing of Sterilizers listed in Appendix A.

1.05 The Employer shall be the ……

……..NHS Trust /Health Employer

1.07 The Project Manager shall be

……

4. CONTRACT RATES AND PRICES

Refer to:

4.01/4.02 Applies/Does not apply*

The following shall be read in conjunction with the Particular Specification of Contract.

7. SECURITY AND PUBLIC HEALTH PRECAUTIONS

Refer to:

7.01 areas subject to special security precautions:

……

……

7.02 Areas subject to special Public Health precautions:

……

……

10. REQUISITIONING OF WORKS

Refer to:

10.1 Local liaison Personnel

……

……

* Delete whichever is not to apply.

PARTICULAR SPECIFICATION FOR THE ANNUAL

TESTING OF STERILIZERS

PARTICULAR SPECIFICATION

1. REGULATIONS

All work shall be carried out in accordance with.

1.01 All relevant Acts or Parliament, statutory instruments and regulations.

1.02 Any public health, security and conduct requirements as from time to time be issued to the Contractor by the Employer.

1.03 Any relevant Safety Regulations published by the Employer copies of which are available from the Project Manager.

2. COMPLIANCE WITH BRITISH STANDARDS

2.01 All work and material shall company with relevant European and British Standards and Codes of Practice.

3. RESPONSIBILITIES OF THE EMPLOYER

The Employer shall be responsible for:

3.01 The keeping of each item of Mechanical and Electrical Plant in such a condition that its functions in accordance with the requirements of SHTM 2010, BS 3970, BS 2646 and BS 3421.

3.02 Arranging for statutory inspections to be carried out (under a separate contract).

3.03 Maintenance of a record for each item of Mechanical and Electrical Plant in accordance with the requirements of SHTM 2010.

This shall contain details of all maintenance and remedial works carried out on each item of equipment to the following standards:

A.	Failures	Date Symptoms of failure
B.	Visits by other Contractors	Date Details of Work carried out including details of tests and replacements. Date and time of completion
C.	Statutory Inspections	Date Details of any remedial work required. Signature of competent person carrying out inspection.

4. INSTRUCTIONS

4.01 The Person from whom the Contractor will be required to accept instructions and attend any urgent or necessary recommissioning is listed in the Abstract of Particulars.

4.02 All requisitions for emergency action will be made by telephone to the Contractor's office or central control point and will be confirmed in writing within 7 days by the Project Manager.

5. DOCUMENTATION

5.01 The Contractor must ensure that on each occasion his staff enter the details of any work carried out on the plant in the Plant History Record before leaving the site.

5.02 The Contractor, within 14 days of the completion of the tests, shall supply the Project Manager with a Test Report carried out under this contract as detailed in Appendix D, together with 3 copies.

6. DESCRIPTION OF THE WORK

6.0l The Contractor shall undertake annual tests as described in Appendix B – Testing Philosophy & Procedures and Appendix C - Annual Performance Tests on those Sterilizers listed in Appendix A - Sterilizer Inventory.

6.02 The Contractor shall employ persons, experienced, qualified and preferably certified to a minimum City and Guilds standard, who would be competent to perform all the required tests, documentary evidence of this shall be provided. The Employer may require the said persons to demonstrate his/her competence by performing a test laid down by the Project Manager, to be witnessed by Project Manager or his/her nominated representative, prior to the letting of the Contract or during the period of the Contract.

6.03 The Contractor shall demonstrate that he has all the necessary equipment which is detailed in Part 3, Paragraph 6.1 – 6.63 of the current edition of Scottish Health Technical Memorandum 2010 (SHTM) and either evidence of its calibration or the means of verifying its calibration.

Current certification of accuracy traceable to the National Physical Laboratory and where appropriate to NAMAS Standards will be required.

6.04 The Contractor shall prepare a schedule of the order and time in which he would perform the tests on the Sterilizers listed in Appendix A, to be agreed by the Project Manager prior to the awarding of the Contract.

6.05 The Contractor will confirm his intention to perform the scheduled test with the Project Manager or his/her nominated representative 14 days in advance.

6.06 The Project Manager or his nominated representative will arrange for the Local Maintenance Engineer to be available to rectify any faults which the Contractor identifies during the test.

6.07 The Contractor shall on completion of an annual test, make a signed and dated entry in the Plant History Record that the Sterilizer complies or does not comply, with the performance requirements. In the event of non-compliance the Contractor shall notify the Project Manager or his local nominated representative (normally a departmental manager) within 24 hours.

6.08 The Contractor shall issue to the Project Manager, or his/her nominated representative, within 21 days of any test being carried out, the results of the tests in a test report as demonstrated in Appendix D together with 3 copies.

6.09 The Contractor shall satisfy himself from the Plant History Records of each Sterilizer give the service maintenance records, and where appropriate, the microbiological records for all routine tests and ascertain they have been performed on each Sterilizer throughout the previous year and is in a condition in which tests can be undertaken safely. Comments shall be included in the Test report.

6.10 The Contractor shall nominate on Appendix 2: Schedule of Contractor's Particulars a representative who will act for the Contractor to liaise with the Project Manager on all matters relating to the Contract.

6.11 The Project Manager will take up any problems of the Contract with the Project Manager or his/her nominated representative.

6.12 The Project Manager or his/her nominated representative may visit any site at any time to inspect the Contractor's test procedures and results.

6.13 The Contractor when requested, on the appropriate form (See Appendix E) will be required to retest any sterilizer that has not satisfactorily passed the annual test criteria.

Repeat tests will be paid for at not more than the cost of the test original of the said Sterilizer as listed in Appendix A, unless investigative testing has been previously agreed.

6.14 The Contractor shall confirm a date for retesting of sterilizers within two days of receiving the request and should carry out the retesting of Sterilizers where applicable within 10 working days of receiving the request.

Appendix A

STERILIZER INVENTORY AND UNIT COSTS

STERILIZER INVENTORY AND UNIT COSTS

……NHS TRUST OR EMPLOYER											
No.	**Location**	**Department**	**Make**	**Col. Model**	**Serial No.**	**Type**	**Periodical /Yearly**	**Date to be undertaken**	**Normal hours**	**Out of hours**	**Unit cost £**
1											
2											
3											
4											
5											
6											
7											
8											
9											
10											
11											
12											
13											
14											
15											
16											
17											
18											
19											
20									TOTAL		

Appendix B

TESTING PHILOSOPHY AND PROCEDURES

TESTING PHILOSOPHY & PROCEDURES

The Testing of Sterilizers required under the contract are those called for in the Scottish Health Technical Memorandum No. 2010, Part 3 (SHTM 2010).

The relevant clauses required for the execution of this contract in fulfilling the procedures for annual testing are presented in full in Appendix C.

Calibration of Instruments

It is the Contractors responsibility to ensure that all instruments used in executing the work are suitably calibrated and hold current certificate of calibration clearly traceable to National Physical Laboratory, British Accreditation Service and that the test system calibration is checked immediately before and immediately after each annual test and is recorded and included in each Test Report. Copies of current certificates are to be forwarded to the Project Manager.

Test Equipment

The relevant clauses required for compliance of equipment used for sterilizer testing are those called for in the Scottish Health Technical Memorandum No. 2010 Part 3 (SHTM 2010) Chapter 6.

Appendix C

ANNUAL PERFORMANCE TESTS

YEARLY AND REVALIDATION TESTS

The tests are listed in the Scottish Health Technical Memorandum 2010, Part 3, Chapters 7 – 19.

The results of tests done should be recorded in the Plant History Record for each sterilizer in the form of a report as described in Appendix D.

This contract requires the yearly tests to be carried out only on those Sterilizers which are listed in SHTM 2010, Part 3, Chapters 4-5 (Check the relevant detail in Schedule of periodic tests to establish those tests only required for yearly testing in the tables).

The Contractor shall include in his report to the Project Manager if he becomes aware that the daily, weekly or quarterly tests have not been satisfactorily carried out. The contractor should be satisfied that the sterilizers are in a condition in which the tests can be undertaken safely.

Schedule of Periodic Tests. Reference SHTM 2010 Part 3.

REFERENCE SHTM 2010 PART 3 SCHEDULE OF TESTS		
STERILIZER PROCESS TYPE	**CHAPTER**	
	4	**5**
	VALIDATION TABLE	**PERIODIC TEST TABLE**
Porous load	2a	4a
Fluids	2b	4b
Unwrapped Instrument and Utensil	2c	4c
Dry Heat	2d	4d
Low Temperature Steam	2e	4e
Low Temperature Steam and Formaldehyde	2e	4e
Ethylene Oxide	2f	4f
Laboratory	3a	5a
Laboratory Culture Media Preparators	3b	5b

Appendix D

REPORTS

REPORTS

Each annual test carried out must be fully reported in the format shown.

Each report will consist of:

1. Title page with details of NHS Trust or Hospital, Department, Manufacturer, Sterilizer type, References and date of test and person(s) carrying out the test.
2. Sequence Test Sheet listing each test carried out, a brief statement on test result and any adjustments or actions taken.
3. Test Report Sheet giving detailed analysis of the test carried out with a conclusion and recommendations.
4. Test Sheets showing details of test carried out (See specimen test sheets).

NOTE: Test sheets may be replaced by suitable computer printouts providing they are authorised by Project Manager.

5. Associated test recorder thermocouple charts, including calibration checks, sterilizer recorder charts, and/or print-outs, Bowie/Dick sheet where applicable. All annotated and suitably identified.
6. Each reports must be suitably bound and forwarded to the Contract Administration together with 2 copies – charts need only be incorporated into the original report.

1. Title page

STERILIZER ANNUAL TEST REPORT

NHS TRUST/EMPLOYER .....

HOSPITAL .....

DEPARTMENT .....

MANUFACTURER .....

MACHINE TYPE .....

REFERENCE .....

FILE REF .....

TEST DUE NO LATER THAN .....19……..

DATE OF TEST .....

TEST CARRIED OUT .....

SIGNATURE .....……..

2. TEST SEQUENCE SHEET

. . . . . NHS TRUST/EMPLOYER

Hospital: **Department:** **Date Tested:**

Manufacturer: **Ref No:** **Our Ref or File No:**

SEQUENCE OF TEST

No.	Test Undertaken	Pass/Fail	Comments Brief Statement
1.			
2.			
3.			
4.			
5.			
ETC.			

3. TEST REPORT SHEET

. . . . . .NHS TRUST/EMPLOYER

Hospital:	**Department:**	**Date Tested:**
Manufacturer:	**Ref No:**	**Our Ref or File No:**

1. DETAIL REPORT

Detailed report of findings as to conforming to standards, faults found, action taken, and recommendations.

2. RECORDS

SHTM 2010 APPENDIX 3. Thermometric Charts/Data Logged/Summary Sheets for process type
Statement on findings of Plant History Record regarding Maintenance and Periodic Testing status.

3. CONCLUSIONS

Brief statement from above detailed report.

4. TESTER'S NAME

……

5. TESTER'S SIGNATURE

……

6. DATE

……

4. SPECIMEN TEST SHEETS REFERENCES

Unwrapped Instrument & Utensil Sterilizer	REF 46/130V
Porous Load Sterilizer	REF 46/129V
Fluids Sterilizer	REF 46/132V
Dry Heat Sterilizer	
Laboratory	REF 46/133

LOW TEMPERATURE STEAM WITH AND WITHOUT FORMALDEHYDE

Full logbooks including inspection, test and maintenance recording facilities for porous load, unwrapped instruments and utensils, laboratory, fluid and dry heat sterilizers are available from:

Printing Services,
Scottish Healthcare Supplies
Trinity Park House
South Trinity Road
EDINBURGH
EH5 3SH
Tel. 0131 552 6255
Fax 0131 552 6536

LABORATORY – MEDIA

Appendix E

RETEST REQUEST FORM

STERILIZER PERIODIC TESTING

REQUEST FOR RETEST

CONTRACT NO……..

Request for Retest Form No……

FROM:……NHS TRUST

TO:……..CONTRACTS

Request for retesting following rectification of faults:

Trust / Employer	……
Hospital	……
Clinic	……
Sterilizer	……
Plant No.	……
Department	……
Room Number	……

Signature of Contracts Manager or Contractor's Representative:……

Date of request:……

Note: The retesting following any remedial works shall be carried out within ten working days of receiving notice, unless requested later.

Section E

Procedures for determining the sound power generated by a sterilizer

Contents

E. Procedures for determining the sound power generated by a sterilizer

Introduction

E.1 This test, to be carried out by the manufacturer of a sterilizer, is based on the test in Appendix D of BS 3970: Part 1: 1990 and in Section 23 of EN 285.

E.2 Except where otherwise stated here, the sound power levels of sterilizers are determined by the method described in BS 4196: Part 6: 1981 (equivalent to ISO 3746: 1979) The information given here is by itself not sufficient to permit the test to be carried out by personnel unfamiliar with the requirements of BS 4196.

E.3 Measurements made by this method have a standard deviation of up to 5 dB for discrete tone sources and up to 4 dB for wide-band noise sources. The uncertainties can be minimised by careful consideration of the conditions in which the test is carried out.

a. The environmental correction factor, K, depends on the relative sizes of the sterilizer and the test room and the sound absorbing qualities of the room. For a given sterilizer, the larger the room the smaller the value of K. Although EN 285 specifies that K should be less than 7 dB, this is a relatively high value and the manufacturer should aim to achieve K = 2 dB or less. This figure can normally be achieved by carrying out the test in a sufficiently large room. The assembly hall in which the sterilizer is constructed should be suitable;

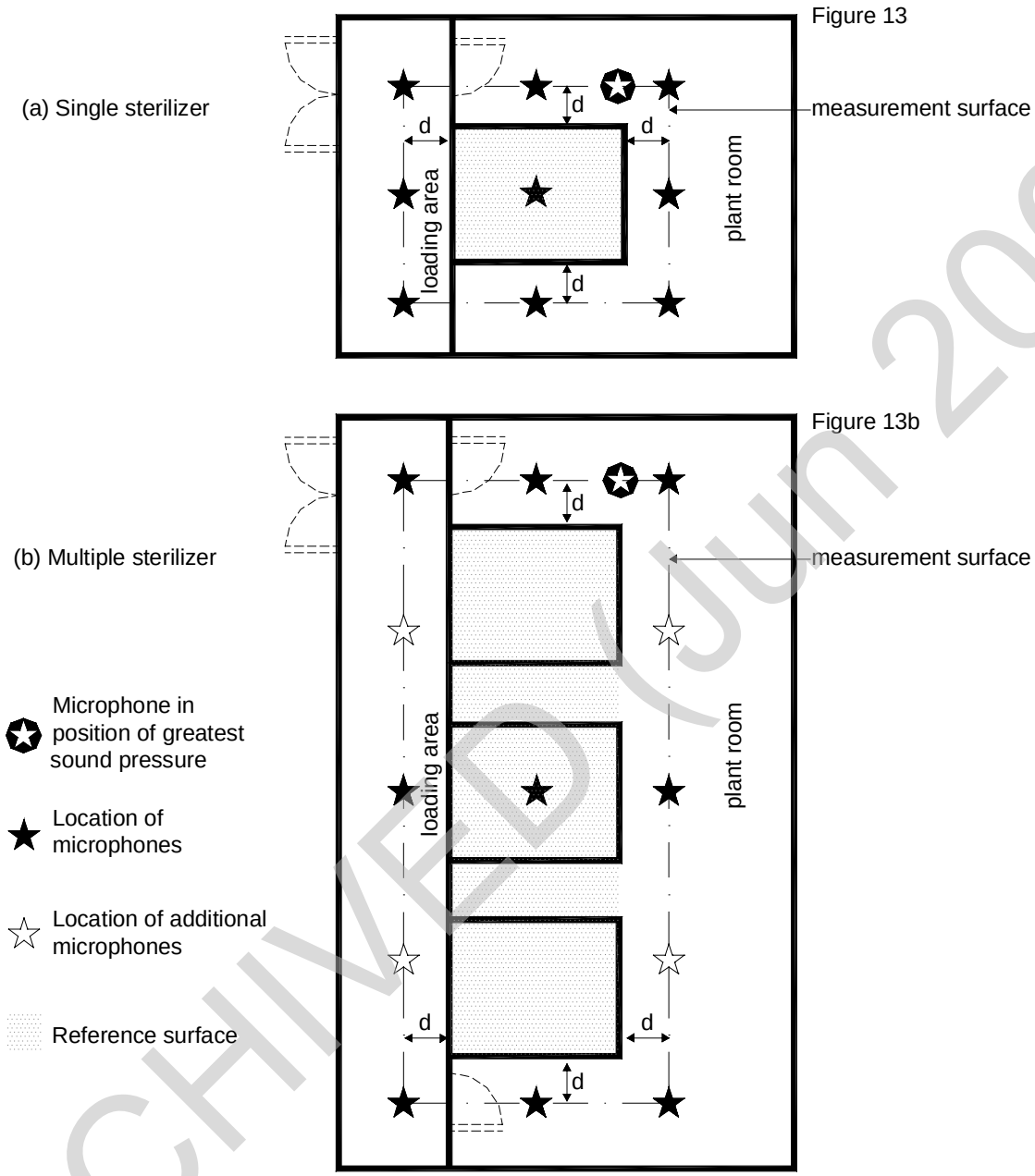
b. Another source of error is the ambient background noise. Table 4 of BS 4196: Part 6 gives correction factors for different levels of background noise, but the lower the correction factor the more reliable the result will be. The correction is essentially zero if the background noise level is 10 dB or more below the level measured when the sterilizer is operating. It should be possible to achieve this on the manufacturer's premises if the test is carried out when the factory is closed and all other plant is shut down. Steam and compressed air plant not part of the sterilizer should be run on storage during the test, with boiler feed pumps and compressors switched off.

Apparatus

E.4 Sound-level meter, complying with type 1 of EN 60651: 1994, or an integrating-averaging sound level meter complying with type 1 of EN 60804: 1994. The sound power level is determined from at least six microphone positions (Figure E1). If the sound meter has insufficient input channels, additional instruments and/or repeated operating cycles are required.

E.5 Test room, configured so that the distance between any wall or other object in the room is not less than 3 m from any reference surface (see paragraph E.6) on the sterilizer to be tested. The room in which the sterilizer is assembled may be suitable providing the conditions discussed in paragraph E3 are met.

Figure E1: Location of microphones for sound pressure test



Test procedure

E.6 The test determines the A-weighted sound power using a rectangular measurement surface. The “reference surface” defined in BS 4196: Part 6 is the smallest rectangular box that just encloses the sterilizer, with a width and depth measured from the outside of the vessel lagging and a height measured from the floor to the top of the vessel lagging. The box does not include pipes and valves used to connect the sterilizer to its services.

E.7 Determine the sound absorption area, A, of the test room using the experimental method described in A.3.1.2 of BS 4196: Part 6. The method of estimation described in A.3.1.1 may be used as a check.

E.8 Determine the environmental correction factor, K, as described in A.3.1 of BS 4196: Part 6. Although EN 285 allows K to be as high as 7 dB, a figure of around 2 dB should be achievable as described in paragraph E.3a.

E.9 Sterilizers should be regarded as “large sound sources” as defined in 7.4.3.2 of BS 4196: Part 6. The measurement distance, d, should be 1.0 ± 0.1 m. Microphones should be placed on the measurement surface as described in 7.4 of BS 4197: Part 6. At least six microphones will be required.

E.10 The test is to be carried out with all integral equipment (for example, water pumps, vacuum pumps, compressors) operating normally.

E.11 Load the sterilizer with a full load as described in Part 3 of this SHTM. If there is a choice of operation cycle, select the cycle with the highest sterilization temperature. Ensure that the pressure and flow from the steam and water services are set to levels which cause the maximum noise and are within the ranges specified for normal operation. Start the operating cycle.

E.12 Using the procedure for measuring the rectangular measurement surface described in BS 4196: Part 6, determine the A-weighted sound power level and the peak sound power level of the sterilizer either for one complete operating cycle or for a 30 min period that contains the most prominent sounds.

Test result

E.13 Record the calculated mean and peak A-weighted sound power levels in decibels to the nearest integer. Other information should be recorded in accordance with BS 4196: Part 6.

E.14 The test should be considered satisfactory if the peak A-weight sound power level at no time exceeds the mean A-weighted sound power level by more than 15 dB.

Section F

Accommodation for ethylene oxide gas cylinders, manifolds and canisters

Contents

F. Accommodation for ethylene oxide gas cylinders, manifolds and canisters

General

F.1 For use in large sterilizers operating at above atmospheric pressure, ethylene oxide is mixed with carbon dioxide or chlorofluorocarbon. Given recent concerns about environmental issues however, the use of the latter is deprecated and is no longer in widespread use. The cylinders therefore are less hazardous than those of pure ethylene oxide.

F.2 Single-shot cartridges of pure ethylene oxide for use in sub-atmospheric pressure machines require care but in view of the modest volumes involved do not pose a major safety problem.

Ethylene oxide cylinders

F.3 Cylinders are categorised in accordance with Table F1 and, although ethylene oxide is supplied in mixture with inert gas, they should be stored under the toxic and/or corrosive and flammable category.

F.4 Cylinders may be stored with other industrial and medical gas cylinders in accommodation designed in accordance with SHTM 2022.

General principles

F.5 Accommodation should be well ventilated and labelled clearly to describe the gases contained. The labelling should include details of emergency action procedures and the location of keys should be identified. Cylinder storage should be designated as a “no smoking” area and appropriate labels should be posted.

F.6 Clear and secure and access is required to permit safe cylinder loading/unloading and handling with vehicular access.

F.7 The maximum temperature in the cylinder store should be that recommended by the gas supplier/manufacturer. Normally this should not exceed 38°C.

F.8 Accommodation should be free from naked flames and sources of ignition and appropriate fire extinguishing equipment should be available. Lighting protection may be necessary for isolated buildings and British Standards CP362 should be consulted.

F.9 For electrical equipment in the vicinity of the gas cylinders the recommendations of BS 5345: 1976, Zone 2 classification will usually be appropriate for the open-air type of installation.

F.10 Safety equipment in the form of protection goggles, gloves and a respirator should be available inside this space and also at the point of entry.

Ethylene oxide cartridges

F.11 Sufficient secure storage within the loading area in the form of a locked cabinet is satisfactory for cartridges for use in a single day.

F.12 Additional cartridges will be required for an operational unit and external storage, for example one week's supply, should be held externally. Small special-purpose cabins typically used for the storage of LPG containers fully protected from the elements will be appropriate.

Table F1: Clarification of gas cylinders typically found on hospital sites

Group classification of gas cylinder contents		Medical gas	Non-medical gas
1	Flammable	Cyclopropane – this is no longer manufactured	Acetylene LPG(eg.. Propane, butane) STG (synthetic town gas) Methane, natural gas, hydrogen
2	Oxidising and/or supports combustion	Medical compressed air Oxygen Nitrous oxide Oxygen/nitrous dioxide Oxygen/carbon dioxide Oxygen/ helium mixtures	Compressed air oxygen Nitrous oxide Oxygen/nitrous oxide mixtures
3	Toxic and corrosive		
3.1	Toxic and/or corrosive and flammable		Ammonia Ethylene oxide (C_2H_4O) Carbon monoxide C_2H_4O/CO_2 mixtures > 6% C_2H_4O
3.2	Toxic and/or corrosive and oxidising		Nitric oxide mixtures Sulphur dioxide Chlorine
3.3	Toxic and/or corrosive only		Ethylene oxide/halo-carbon mixture < 15% C_2H_4O Certain conditions only – ethylene oxide/carbon dioxide mixtures < 6% C_2H_4O
4	Others including inert, but excluding toxic or corrosive	Carbon dioxide Helium	Carbon dioxide Nitrogen Argon Helium Halo-carbon Refrigerants

References

NOTE:
Where there is a requirement to address a listed reference, care should be taken to ensure that all amendments following the date of issue are included.

Publication ID	***Title***	***Publisher***	***Date***	***Notes***
Acts and Regulations				
	Building (Scotland) Act	HMSO	1959	
	Clean Air Act	HMSO	1968	
	Consumer Protection Act	HMSO	1987	
	Electricity Act	HMSO	1989	
	Health and Safety at Work etc Act	HMSO	1974	
	Health and Medicines Act	HMSO	1988	
	Registered Establishments (Scotland) Act	HMSO	1987	
	Water (Scotland) Act	HMSO	1980	
SI 3146	Active Implantable Medical Devices Regulations	HMSO	1992	
SI 2179 & 187	Building Standards (Scotland) Regulations	HMSO	1990	
	Building Standards (Scotland) Regulations: Technical Standards Guidance	HMSO	1998	
SI 1460	Chemicals (Hazard Information and Packaging for Supply) Regulations (CHIP2)	HMSO	1997	
SI 3140	Construction (Design and Management) Regulations	HMSO	1994	
SI 437	Control of Substances Hazardous to Health Regulations (COSHH)	HMSO	1999	
SI 635	Electricity at Work Regulations	HMSO	1989	
SI 1057	Electricity Supply Regulations	HMSO	1988	
SI 2372	Electromagnetic Compatibility Regulations	HMSO	1992	
SI 3080	Electromagnetic Compatibility (Amendment) Regulations	HMSO	1994	
SI 2451	Gas Safety (installation and use) Regulations	HMSO	1994	
SI 917	Health & Safety (First Aid regulations)	HMSO	1981	
SI 682	Health & Safety Information for Employees Regulations	HMSO	1989	

Publication ID	Title	Publisher	Date	Notes
SI 1380	Health and Safety (Training for Employment) Regulations	HMSO	1990	
SI 341	Health and Safety (Signs and Signals) Regulations	HMSO	1996	
SI 2792	Health and Safety (Display Screen Equipment) Regulation (as amended)	HMSO	1992	
SI 2307	Lifting Operations and Lifting Equipment Regulations (LOLER)	HMSO	1998	
SI 2051	Management of Health and Safety at Work Regulations	HMSO	1992	
SI 2793	Manual Handling Operations Regulations	HMSO	1992	
SI 3017	Medical Devices Regulations	HMSO	1994	
SI 1790	Noise at Work Regulations	HMSO	1989	
SI 2966	Personal Protective Equipment at Work (PPE) Regulations	HMSO	1992	
SI 2306	Provision and Use of Work Equipment Regulations (PUWER)	HMSO	1998	
SI 3139	Personal Protective Equipment (EC Directive) Regulations	HMSO	1992	
SI 2169	Pressure Systems and Transportable Gas Containers Regulations	HMSO	1992	
SI 3163	Reporting of Injuries, Diseases and Dangerous Occurrences Regulations (RIDDOR)	HMSO	1985	
SI 119	Water Supply (Water Quality) (Scotland) Regulations	HMSO	1990	
SI 3004	Workplace (Health, Safety and Welfare) Regulation	HMSO	1992	
British Standards				
BS 2646	**Autoclaves for sterilization in laboratories** **Part 1:** Specification for design, construction, safety and performance **Part 2:** Guide to planning and installation **Part 3:** Guide to safe use and operation **Part 4:** Guide to maintenance **Part 5:** Methods of testing for function and performance	BSI Standards	 1993 1990 1993 1991 1993	

Publication ID	*Title*	*Publisher*	*Date*	*Notes*
BS 5304	**British standard code of practice for safety of machinery**	BSI Standards	1988	
BS EN 866	**Biological systems for testing sterilizers and sterilization processes**	BSI Standards		
	Part 1: General requirements		1997	
	Part 2: Particular systems for use in ethylene oxide sterilizers		1998	
	Part 3: Particular systems for use in moist heat sterilizers		1997	
BS EN 30993	**Biological evaluation of medical devices**	BSI Standards		
	Part 3: Tests for genotoxicity, carcinotoxicity, and reproductive toxicity		1994	
	Part 4: Selection of tests for interaction with blood		1994	
	Part 5: Tests for cytotoxicity, in vitro methods		1994	
	Part 6: Tests for local effects after implantation		1995	
BS EN 837-1	**Bourdon tube pressure gauges: dimensions, metrology, requirements and testing**	BSI Standards	1998	
BS EN 50081	**Electromagnetic compatibility. Generic emission standard**	BSI Standards		
	Part 1: Residential, commercial and light industry		1992	
	Part 2: Industrial environment		1994	
BS EN 50082	**Electromagnetic compatibility. Generic immunity standard**	BSI Standards		
	Part 1: Residential, commercial and light industry		1998	
	Part 2: Industrial environment		1995	
BS 5295	**Environmental cleanliness in enclosed spaces**			
	Part 1: Specification for clean rooms and clean air devices		1989	
BS EN 45003	**Calibration and testing laboratory accreditation systems, general requirements for operation and recognition**	BSI Standards	1995	
BS EN 45011	**General requirements for bodies operating product certification systems**	BSI Standards	1998	

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BS EN 45012	**General requirements for bodies operating assessment and certification/registration of quality system**	BSI Standards	1998	
BS EN 45014	**General criteria for supplier's declaration of conformity**	BSI Standards	1993	
BS EN 980	**Graphical symbols for the use in the labelling of medical devices**	BSI Standards	1997	
BS EN 724	**Guidance on the application of EN 29001 and EN 46001 and of EN 29002 and EN 46002 for non-active medical devices**	BSI Standards	1995	
BS EN 60751	**Industrial platinum resistance thermometer sensors**		1996	
BS 3928	**Method for sodium flame test for air filters (other than for air supply to I.C. engines and compressors)**	BSI Standards	1969	
BS EN 867	**Non-biological systems for use in sterilizers** **Part 1:** General requirements **Part 2:** Process indicators **Part 3:** Specification for Class B indicators for use in the Bowie and Dick test	BSI Standards	1997	
BS EN 868	**Packaging materials and systems for medical devices which are to be sterilized. General requirements**	BSI Standards	1997	
BS 2648	**Performance required for electrically heated laboratory drying ovens (PD2517,6/56)**	BSI Standards	1955	
BS EN 764	**Pressure equipment. Terminology and symbols: pressure, temperature, volume**	BSI Standards	1995	
BS EN ISO 9001	**Quality systems. Model for quality assurance in design, development, production, installation and servicing**	BSI Standards	1994	
BS EN ISO 9002	**Quality systems. Model for quality assurance in production, installation and servicing**	BSI Standards	1994	
BS EN 134	**Respiratory protective devices. Nomenclature of components. Names of components in three CEN languages and diagrams for respiratory protective equipment**	BSI Standards	1998	

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BS 7671	**Requirements for electrical installations. IEE wiring regulations**	BSI Standards	1992	16th edition
BS 3693	**Recommendations for design of scales and indexes on analogue indicating instruments**		1992	
BS EN 61010	**Safety requirements for electrical equipment for measurement, control and laboratory use**			
	-1: General requirements		1993	
	-2-041: Particular requirements for autoclaves and sterilizers using steam for the treatment of medical materials and for laboratory processes		1997	
	-2-042: Particular requirements for autoclaves and sterilizers using toxic gas for the treatment of medical materials and for laboratory processes		1997	
	-2-043: Particular requirements for autoclaves and sterilizers using either hot air or hot inert gas for the treatment of medical materials and for laboratory processes		1998	
BS 6001	**Sampling procedures for inspection by attributes**	BSI Standards	1991	
BS 5815	**Sheets, sheeting, pillowslips, towels, napkins and continental quilts secondary covers**	BSI Standards	1989	
	Parts 1: Specification for sheeting etc		1988	
	Part 2: specification for towels etc.		1991	
	Part 3: Specification for counterpanes etc.			
BS EN 45020	**Standardization and related activities**	BSI Standards	1998	
BS 6257	**Specification for paper bags for steam sterilization for medical use**		1989	
BS 6447	**Specification for absolute and gauge pressure transmitters with electrical outputs**		1984	
BS EN 60804	**Specification for integrating averaging sound level meters**		1994	
BS 7720	**Specification for non-biological sterilization indicators equivalent to the Bowie and Dick Test**		1995	

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BS 593	**Specification for laboratory thermometers**		1989	
BS 1781	**Specification for linen and linen union textiles**		1981	
BS 2775	**Specification for rubber stoppers and tubing for general laboratory use**		1987	
BS 5164	**Specification for indirect acting electrical indicating and recording instruments and their accessories**		1975	
BS 3970	**Sterilizing and disinfecting equipment for medicinal products**	BSI Standards		
	Part 1: Specification for general requirements		1990	
	Part 2: Specification for steam sterilizers for aqueous fluids in sealed rigid containers		1991	
	Part 3: Specification for steam sterilizers for wrapped goods and porous loads		1990	
	Part 4: Specification for transportable steam sterilizers for unwrapped instruments and utensils		1990	
	Part 5: Specification for low temperature steam disinfectors		1993	
	Part 6: Specification for sterilizers using low temperature steam with formaldehyde			
BS EN 1174	**Sterilization of medical devices. Estimation of population of micro-organisms on product**	BSI Standards	1996	
BS EN 552	**Sterilization of medical devices. Validation and routine control of sterilization by irradiation**	BSI Standards	1994	
BS EN 285	**Sterilization, steam sterilizers, large sterilizers**	BSI Standards	1997	
BS EN 550	**Sterilization of medical devices. Validation and routine control of sterilization by ethylene oxide**	BSI Standards	1994	
BS EN 554	**Sterilization of medical devices. Validation and routine control of sterilization by moist heat**	BSI Standards	1994	
BS EN 556	**Sterilization of medical devices. Requirements for terminally sterilized medical devices to be labelled 'STERILE'**	BSI Standards	1995	

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BS EN 1422	**Sterilizers for medical purposes – ethylene oxide sterilizers – specification**	BSI Standards	1998	
BS EN 46001	**Specification for the application of EN ISO9001 to the manufacture of medical devices**	BSI Standards	1997	
BS EN 46002	**Specification for the application of EN ISO9002 to the manufacture of medical devices**	BSI Standards	1994	
BS EN 60584-1	**Thermocouples reference table**	BSI Standards	1996	
BS EN 60581-2	**Thermocouples. Manufacturing tolerances**	BSI Standards	1996	
BS EN 25667-1	**Water quality. Guidance on design of sampling programmes**	BSI Standards	1994	
BS EN 25667-2	**Water sampling . Guidance on sampling techniques**	BSI Standards	1993	
BS 6068	**Water quality** **Sect.1.2** Glossary **Sect 6.5** Guidance on sampling of drinking water and water used for food processing **Sect. 6.7** Guidance on sampling of water and steam in boiler plants.	BSI Standards	1997 1991 1994	
European Union Directives				
65/65/EEC	Approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products.	Official Journal of the European Communities (OJEC), no 22, 9/2/65, p 369		
75/107/EEC	Approximation of the laws of member states relating to bottles used as measuring containers.	Official Journal of the European Communities (OJEC), L42, 15/2/75		
90/385/EEC	Approximation of the laws of the Member States relating to active implantable medical devices.	Official Journal of the European Communities (OJEC), L189 20/7/90, p 17		
91/356/EEC	Laying down the principles and guidelines of good manufacturing practice for medicinal products for human use.	Official Journal of the European Communities (OJEC). L193 17/7/91, p 30		

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80/778/EEC	Quality of water intended for human consumption	Official Journal of the European Communities, 1980		
93/42/EEC	Medical Devices Directorate	Official Journal of the European Communities (OJEC), L169 12/7/93, p 1		
Scottish Health Technical Guidance				
SHTM 2023	Access and accommodation for engineering services	EEF	1999	CD-ROM
SHTM 2045	Acoustics	EEF	1999	CD-ROM
SHPN 15	Accommodation for pathology services	HMSO	1994	
SHTM 2031	Clean steam for sterilizers	EEF	1999	CD-ROM
SHTM 2040	Control of legionellae in healthcare premises – a code of practice	EEF	1999	CD-ROM
SHTN 2	Domestic hot and cold water systems for Scottish Health Care Premises	EEF	1999	CD-ROM
SHTM 2007	Electrical services supply and distribution	EEF	1999	CD-ROM
SHTM 2011	Emergency electrical services	EEF	1999	CD-ROM
SHTM 2020	Electrical safety code for low voltage systems (Escode – LV)	EEF	1999	CD-ROM
SHTN 4	General Purposes Estates and Facilities Model Safety Permit-to-Work system	EEF	1998	
SHPN 1	Health service building in Scotland	HMSO	1991	
SHPN 2	Hospital briefing and operational policy	HMSO	1993	
SHTM 2027	Hot and cold water supply, storage and mains services	EEF	1999	CD-ROM
SHTM 2022	Medical gas pipeline systems	EEF	1999	CD-ROM
	NHS in Scotland – Scotconcode	EEF	1999	Version 3
SHGN	Pressure Systems and Transportable Gas Containers Regulations 1989	EEF	1999	CD-ROM
SHTN 1	Post commissioning documentation for health buildings in Scotland	HMSO	1993	
SHGN	'Safe' hot water and surface temperatures	EEF	1999	CD-ROM
SHPN 13	Sterile services department	HMSO	1994	
SHTM 2025	Ventilation in healthcare premises	EEF	1999	CD-ROM
SHTM 2030	Washer-disinfectors	EEF	1999	CD-ROM

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NHS in Scotland Firecode				
HTM 82	Alarm and detection systems	EEF	1998	CD-ROM
Fire Practice Note 6	Arson prevention and control in NHS healthcare premises	EEF	1998	CD-ROM
Fire Practice Note 5	Commercial enterprises on hospital premises	EEF	1998	CD-ROM
Fire Practice Note 3	Escape bed lifts	EEF	1998	CD-ROM
HTM 81	Fire precautions in new hospitals	EEF	1998	CD-ROM
HTM 85	Fire precautions in existing hospitals	EEF	1998	CD-ROM
Fire Practice Note 7	Fire precautions in patient hotels	EEF	1998	CD-ROM
HTM 86	Fire risk assessment in hospitals	EEF	1998	CD-ROM
HTM 83	Fire safety in healthcare premises: general fire precautions	EEF	1998	CD-ROM
HTM 84	Fire safety in NHS residential care properties	EEF	1998	CD-ROM
Fire Practice Note 4	Hospital main kitchens	EEF	1998	CD-ROM
Fire Practice Note 10	Laboratories on hospital premises	EEF	1998	CD-ROM
HTM 87	Textiles and furniture	EEF	1998	CD-ROM
UK Health Technical Guidance				
HTM 2014	Abatement of Electrical Interference	HMSO	1993	
HBN 29	Accommodation for pharmaceutical services	HMSO	1988	
HTM 67	Building components: laboratory fitting out system	HMSO	1993	
CONCODE	Contracts and commissions for the NHS estate – contract procedures	HMSO	1994	
MES	Model Engineering Specifications	NHS Estates	1997	As required
MES C14	Sterilizers	NHS Estates	1993	
HBN 13	Supplement 1 - Ethylene oxide sterilization section	HMSO	1994	
MES C02	Thermal insulation	NHS Estates	1993	
Health and Safety Guidance				
EH 40	HSE Occupational Exposure limits	HSE	Annual	

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HN(76)126	Hospital design note 4 (noise control): amendments to appendices II, IV and VII	DHSS	1976	
STB3A/85/12	Performance and safety specification for media sterilizers. Media devices directorate	DHSS	1985	
	Emmerson, A. M. *Sterilization, disinfection and cleaning of medical equipment: guidance on decontamination from the Microbiology Committee to the Department of Health Medical Devices Directorate.* Medical devices directorate	Department of Health	1993	
	Biological tests for graded milk. Memo 139/Foods.	Ministry of Health	1937	
	Scottish Infection Manual Guidance on the core standards for the control of infection in hospitals, healthcare premises and at the community interface	The Scottish Office	1998	
HS(R) 30	*A guide to the pressure systems and transportable gas container regulations*	HSE	1989	
	Programmable electronic systems in safety related applications: General technical guidelines	HSE	1987	
	Programmable electronic systems in safety related applications: an introductory guide	HSE	1987	
L 5	General COSHH ACOP (Control of substances hazardous to health) Carcinogens ACOP (Control of carcinogenic substances) and Biological agents ACOP (Control of biological agents) Control of Substances Hazardous to Health Regulations1999 Approved Code of Practice	HSE	1999	
L 22	Safe use of work equipment: Approved code of practice and guidance	HSE	1998	
L 23	Manual handling operations: guidance on regulations	HSE	1998	
L 24	Workplace health, safety and welfare: Approved code of practice and guidance	HSE	1992	
L25	Personal protective equipment at work at work: guidance on regulations		1992	
L113	Safe use of lifting equipment: Approved code of practice and guidance	HSE	1998	
COP 37	Safety of pressure systems.: Approved code of practice	HSE	1990	
COP 38	Safety of transportable gas containers: Approved code of practice	HSE	1990	

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Miscellaneous References				
	Atomic absorption spectrophotometry 1979 version	HMSO	1979	(out of print)
	Cadmium in potable waters by atomic absorption spectrophotometry 1976	HMSO	1976	(out of print)
	Colour and turbidity of waters 1981	HMSO	1981	(out of print)
	Determination of anions and cations, transition metals, and other complex ions and organic acids and bases in water by chromatography 1990	HMSO	1990	
	Lead in potable waters by atomic absorption spectrophotometry 1976	HMSO	1976	(out of print)
	Lead and cadmium in fresh waters by atomic absorption spectrophotometry (second edition) a general introduction to electrothermal atomization atomic absorption spctrophotometry 1986	HMSO	1986	(out of print)
	Measurements of electrical conductivity and the laboratory determination of the pH value of natural, treated and waste waters.	HMSO		(out of print)
	Mercury in waters, effluents, soils and sediments etc, additional methods	HMSO	1985	(out of print)
	Phosphorus and silicon in waters, effluents and sludges 1992	HMSO	1993	
	Model Water Byelaws: Dept. of the Environment	HMSO	1986	
LG 2	Lighting guide: hospitals and healthcare buildings	Chartered Institution of Building Services Engineers	1989	
	Sterilization and disinfection of heat-liable equipment	Central Sterilizing Club	1986	