What on Earth is going on?

Controversy on porous load cycles

by Alan Heavey

- ★ A change in the definition of a reference measurement point in BS EN 285:2006 + A1: 2008 is causing concern
- ★ Various ways in which this change of wording can be interpreted mean that the efficacy of sterilization could be compromised

Introduction

For many years there has been an 'Acceptance Criterion' for Porous Load/Hardware autoclave cycles, known as the 'Equilibration Time'. Anyone working in the UK or having their products licensed through the UK shudders when this term is mentioned because for many it has been a difficult criterion to meet. If the criterion is not met, it indicates poor air removal from within the autoclave load, typically caused by inefficient cycle design or load configuration, packaging issues, difficult to sterilize items, incorrect placement of test thermocouples and biological indicators, etc. or a combination of these factors.

The acceptance criterion in question is – *'The equilibration time shall not exceed 15 s for sterilizer chambers up to 800 l usable space and 30 s for larger sterilizer chambers'* (BS EN 285:2006+A1:2008).

HTM 2010

The term, 'Equilibration Time' came from *Health Technical Memorandum 2010*, commonly referred to as HTM 2010. Although it is a guidance document, originally introduced for the UK National Health Service (NHS), it has been widely used by companies in the Pharmaceutical and Biotech industry and Regulatory Authorities, some to a greater degree than others. This usage has not been restricted to the UK; its impact has been worldwide.

Let's look at how HTM 2010 defines 'equilibration':
HTM 2010 Part 3 – *'The period which elapses between the attainment of the sterilization temperature in the chamber and the attainment of the sterilization temperature in all parts of the load (see paragraph 7.10).'*

Paragraph 7.10 states:
'The holding time is preceded by a period in which the sterilization conditions are present in the chamber but not yet present throughout the load. This is known as the equilibration time.'

For a better understanding of the rationale of this definition we need to look at Sections 7.16 and 6.26-6.27.

Section 7 is titled, 'Testing methods', and discusses general principles and methods used in the thermometric and microbiological tests described in the HTM. Section 6 is related to 'Test equipment', defined as, portable test equipment required to carry out test procedures described within HTM 2010. **So, the temperatures used to calculate 'equilibration time' are measured by thermocouples attached to a data logger, not by autoclave control probes**.

Let's continue by looking at Section 7.16:
7.16 – *'The equilibration time begins when the temperature in the coolest part of the chamber (normally the active chamber discharge, see paragraph 6.26) first attains the sterilization temperature. It ends when the holding time begins.'*

Now we go to Section 6.26 and 6.27:
6.26 – *'Many of the tests require a temperature sensor to be placed in the active chamber discharge of the sterilizer. This is a drain or vent which permits the controlled flow of air and condensate (a drain) or of air alone (a vent), such that the temperature within the discharge is the same as the chamber temperature.*

The preferred locations are as follows:

a. in the drain, if it is active throughout the operating cycle;
b. otherwise in a vent, if it is active throughout the operating cycle;
c. otherwise in the coldest part of the usable chamber space.'

… such that the temperature within the discharge is the same as the chamber temperature, – **is a very important point to remember**. In other words, it is expected that the temperature measured in the drain is the same as the chamber temperature, as inferred in Section 6.27.

6.27 – *'The sensor should be placed in the drain or vent in steam phase boundary conditions in a position where overheat cannot be detected. This will normally require at least 10mm insertion depth. The sensors connected to*

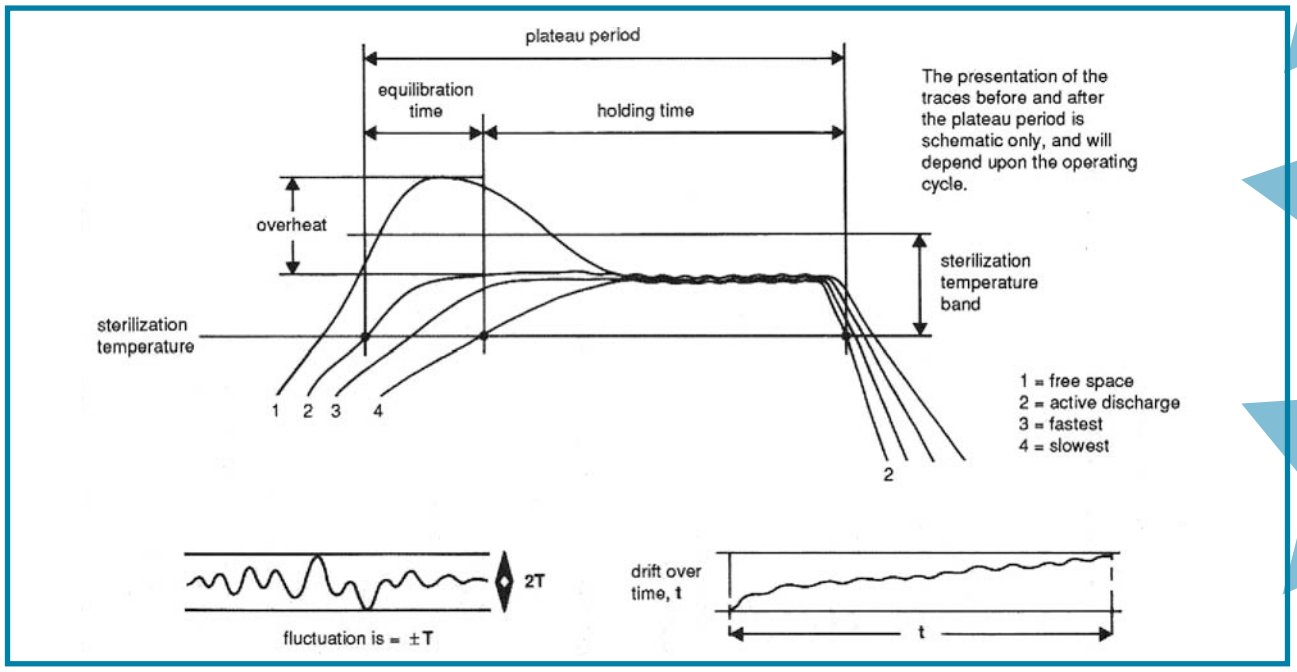
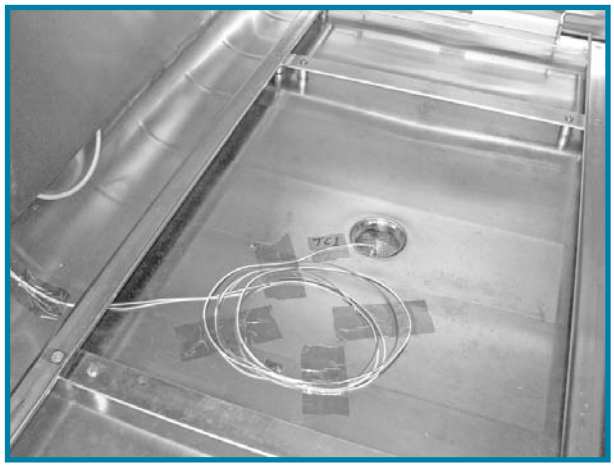


Figure 1. Demonstration of equilibration time and sterilization temperature.

Figure 2. Thermocouple 2 inserted into the chamber drain.



the sterilizer temperature indicator and recorder, and to the automatic controller, are normally in this position also. Care should be taken to ensure that the sensor does not touch any metal parts. (Contact between the hot junction and metal surfaces can cause induced electromotive forces [EMFs] leading to inaccurate readings.)'

An NHS dedicated Porous Load autoclave typically has a drain control probe in this position (unlike some autoclaves I have seen worldwide, which have been positioned in the region of 3m from the chamber drain). Therefore this equilibration time criteria was not difficult to achieve as the autoclave cycle was designed to attain it.

Figure 1. from HTM 2010 helps us understand this interpretation of 'equilibration time'. The 'equilibration start point' begins when thermocouple 2 in the diagram, (which is typically inserted 100mm [4"] into the chamber drain as can be seen from **Figure 2**) attains the sterilization temperature. I wouldn't use thermocouple 2 in the drain; in reality it makes more sense to use thermocouple 1 and then position the other thermocouples throughout the chamber and load.

The 'equilibration end point' occurs when the last load thermocouple reaches sterilization temperature (thermocouple 4 in the diagram). This difference in time is called the 'equilibration time'.

BS EN 285:1997

'BS EN 285:1997 Sterilization – Steam sterilizers – Large sterilizers' also discussed 'equilibration time'.

It is the English version of the European EN 285 standard, and draws attention to the guidance contained within HTM 2010. In Section 3.15 we see the definition of 'equilibration time' – *'Period which elapses between the attainment of the sterilization temperature in the sterilizer chamber and the attainment of the sterilization temperature at all points within the load (EN 554).'* The definition refers to EN 554, 'Sterilization of medical devices – Validation and routine control of sterilization by moist heat.' EN

544 has since been replaced by BS EN ISO 17665-1:2006.

The 'reference measurement point' is defined in Section 3.26 as – *'Reference point for which documented evidence is available to demonstrate that it has a known relationship to the temperature of the coolest part of the sterilizer chamber.'*

This 'reference measurement point' refers to a position where a temperature is 'measured'. 'Measured' temperature refers to a thermocouple connected to a data logger. 'Recorded' temperature refers to a recorder attached to the autoclave, whilst 'indicated' refers to a temperature indicator on the autoclave.

For confirmation of the 'measured' link between 'equilibration' and the 'reference measurement point', paragraph 2 of Section 8.3.1.2 states. *'During the plateau period, the temperature measured above a standard test pack (see 18.1) shall not exceed the temperature measured at the reference measurement point of the sterilizer chamber by more than 5 K for the first 60 s and 2 K for the remaining period.'*

This clearly infers that the 'measured temperature' is obtained by thermocouples; one positioned in the 'reference measurement point' and another above the standard test pack. At least one thermocouple is positioned within the test pack (in practice I would use more than one). This relationship between the 'reference measurement point' and thermocouples is mentioned several times in BS EN 285:1997 as it is in HTM 2010. In practice a thermocouple is always positioned in the drain at a depth of 100mm or 4", in a position known as the, 'phase boundary condition'. This is a direct reference to Section 6.27 in HTM 2010 (see above). This is how it has been done in my experience for over 30 years and is what I would expect to see when auditing validation and qualification data.

BS EN 285:2006+A1:2008

So far so good – then along came, *'BS EN 285:2006, followed by, BS EN 285:2006+A1:2008 Sterilization – Steam sterilizers – Large sterilizers'.*

A change in the wording of this document has caused utter confusion, not only in interpretation but also in action. The change appears in the revised definition for the 'reference measurement point', which is now defined in Section 3.26 as, *'point where the temperature sensor for the sterilization cycle control is located'*.

Remember in the 1997 version of BS EN 285 it is defined in Section 3.26 as – *'Reference point for which documented evidence is available to demonstrate that it has a known relationship to the temperature of the coolest part of the sterilizer chamber.'*

This is the first point of my concern, ie. these two points are not necessarily going to be the same. Indeed if the temperature sensor for the sterilization cycle control is 3m away from the chamber drain, it can't represent the coolest part of the sterilizer chamber as it's nowhere near the chamber.

Does it matter if the test thermocouple is 3m from the chamber?

Imagine this scenario:

You have an autoclave where the temperature sensor for the sterilization cycle control is 3m away from the chamber drain. During Qualification studies you have positioned thermocouple 1, 100mm in the drain, ie. 'phase boundary condition'. Some of the load thermocouples are positioned in silicone tubing which has been double packaged before placement on the autoclave trolley. When thermocouple 1 reaches 121.0°C (249.8°F), the 'equilibration start point' is reached. 1 minute 30 seconds later two of the load thermocouples within the silicone tubing have only just reached 121.0°C (249.8°F). Therefore the Acceptance Criterion has not been met as the limit was 30 seconds. Quite clearly there is a problem. However, doesn't the latest BS EN 285 suggest putting thermocouple 1 in the position where the temperature sensor for the sterilization cycle control is located? So you take thermocouple 1 and reinsert 3m down the drain line alongside the drain probe sensor.

You then resume the Qualification studies and the 'equilibration time' is now 20 seconds. You have just qualified the load including the silicone tubing. However, consider what has happened here. The initial Qualification run failed due to poor air removal from within the tubing as indicated by the equilibration time of 1 minute 30 seconds. Repositioning thermocouple 1 has not improved the air removal from the tubing. The reason for appearing to pass the criterion was its positioning 3m away. It took longer for thermocouple 1 to reach the 'equilibration start point' and by doing so gave an extended time for the thermocouples within the tubing to reach the sterilization temperature. The problem wasn't solved, just masked. This is a real example.

My second point of concern is based on how individuals, auditors and Regulatory Authorities are interpreting this new definition in BS EN

285:2006+A1:2008. For example, I am aware of one instance where a Pharmaceutical company was told during a Regulatory Inspection that the 'equilibrium time' should be taken from when the autoclave drain/active discharge probe exceeds temperature, not when the test thermocouple located within the drain reaches temperature. This is a dangerous position to take – if you follow my reasoning above and read the documents quoted, I fail to see how anyone can reach that interpretation. Also the 'drain probe' sensor is typically a 'resistance temperature detector' (RTD) and will often have a slower response rate than a thermocouple; meaning that the 'equilibration start point' would take even longer to attain.

The 'reference measurement point' must be representative of the coolest part of the chamber, ie. 100mm down in the drain, and the measurement taken from the temporary test thermocouple at that point, not the autoclave drain sensor itself, otherwise how could the data be interpreted accurately and meaningfully? This becomes quite clear when referring to BS EN 285:2006+A1:2008, Annex D – 'Temperature and time tolerances during the small load thermometric test.'

Summary

The question I'm asking is, 'How on earth did we get into this situation?'

The 'reference measurement point' is also mentioned several times in 'ISO 17665-2:2009', guidance on the application of 'BS EN ISO 17665-1:2006 Sterilization of health care products – Moist heat – Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices'.

The understanding and implication of 'Equilibration Time' is hugely important for all involved in 'Moist Heat Sterilization'. Unless correct interpretation and judgements are made, the efficacy of sterilization could well be compromised.

I will continue to advise, 'Good Practice and Excellence', based on science, my knowledge and experience. If we are not careful the industry could be going down the 'An accident waiting to happen' road. No one wants to go down that road including me.

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