WHY IS AIR REMOVAL SO CRITICAL TO EFFECTIVE STEAM STERILISATION?

WHY IS IT THAT SOME EU REGULATORY AGENCIES REGARD THIS AS SUCH A BIG ISSUE, WHILST OTHERS FAIL TO SEE THE IMPORTANCE?

There are many examples of differences in detail between EU and US GMP expectations, but one of the biggest and most important concerns air removal in steam sterilisation. Why is it that some EU regulatory agencies regard this as such a big issue, whilst others fail to see the importance?

THE IMPORTANCE OF AIR REMOVAL

To achieve effective steam sterilisation, dry saturated steam must contact the surfaces to be sterilised so that energy can be transferred. It follows, therefore, that nothing must come between the steam and the surface to be sterilised. Herein lies our major challenge. Most of the equipment we seek to sterilise (filters, tubing, vessels, filling needles, etc) contain vast quantities of air. If this air is not removed, then it can act as an insulating barrier between steam and equipment and thus compromise the sterilising process.

Thus, in the case of equipment sterilisation, the key to effective sterilisation is…

- **total removal of air (and condensate)**
- **complete replacement of air by dry saturated steam**

Hence the emphasis on air removal!

METHODS OF AIR REMOVAL

Equipment is generally sterilised by the use of a so-called "porous load" autoclave cycle, whereby air is removed from the autoclave chamber and load by pulling a vacuum and replacing the vacuum by steam. Generally speaking, a single vacuum pulse, no matter how long in duration, is unlikely to achieve total air removal; a series of vacuum pulses will be necessary. The number and duration of pulses needed to achieve

efficient air removal will be determined by the nature of the equipment to be sterilised and the way it is wrapped. Thus, a 50 litre vessel with a small vent filter attached to it via 1m of 10mm diameter silicone tubing represents a huge challenge to the air removal capability of the autoclave as all the air must be drawn out of the vessel and tubing via the small vent filter. Whilst it may be relatively easy to remove air from the autoclave chamber (as measured by the controlling pressure sensor) it will be much more difficult to remove all the residual air from the equipment. Excessive wrapping only exacerbates the problem.

That is why it is so important to optimise the pre-sterilisation phase of the autoclave cycle to ensure…

- **total air removal effective**
- **heating of the load**

Air may be removed by a series of sub-atmospheric (negative) pulses, which draw out air by vacuum and then replace the vacuum with steam up to atmospheric pressure. Such cycles can be effective

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at removing air, but may be less effective at heating the load as the steam never exceeds 100°c. This problem can be overcome by incorporating a series of super-atmospheric (positive) pulses, whereby the chamber is pressurised with steam after a series of vacuum pulses and then evacuated to atmospheric pressure or below. In this way the load can be heated more effectively as the steam will achieve temperatures well in excess of 100°c. Figure 1 shows a typical porous load cycle incorporating both negative and positives pulses.

If the pre-sterilisation phase of the autoclave cycle has been optimised, then transition to the sterilisation phase should result in all pieces of equipment reaching sterilisation temperature simultaneously. EN285 states that, for a typical industrial autoclave, all heat penetration thermocouples distributed within the load, should reach sterilising temperature within 30 seconds. Any delay indicates either a failure to remove air or a failure to adequately heat the load and, as such, the autoclave cycle should be considered unsatisfactory!

It is not enough simply to extend the sterilisation phase until all thermocouples achieve the desired temperature for the required time (as many companies do!) as you may not have saturated steam conditions and so will not achieve effective sterilisation. Rather, you should go back to the pre-sterilisation phase of the cycle and increase the number and/or duration of pulses to achieve the required result.

MEANS OF CONFIRMING EFFECTIVE AIR REMOVAL

There are numerous ways of confirming effective air removal in autoclaves…

- a drain-mounted air detector
- the Bowie-Dick test (or equivalent)
- chamber leak rate test

Air detectors are relatively common on autoclaves in the United Kingdom and Ireland, but less so elsewhere. The device is fitted to the drain of the autoclave and it will not permit commencement of the sterilisation phase of the cycle until the air content in the steam leaving the chamber is below a fixed level.

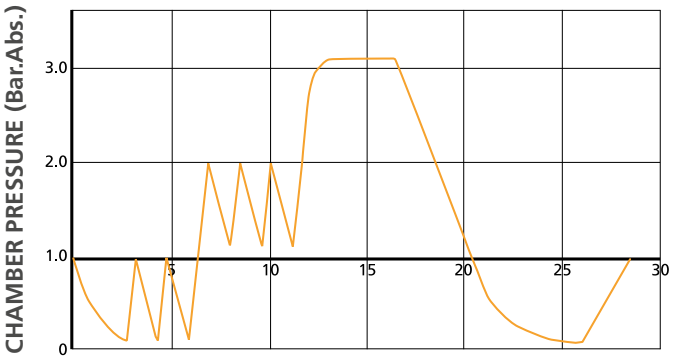

Figure 1. A typical porous load cycle incorporating both negative and positive pulses.

The air detector alone may not be sufficiently sensitive to detect potentially significant levels of air if these are trapped within the load. Thus, a more direct test of air removal from the load is recommended – the so-called Bowie-Dick test pack. This consists of a stack of folded towels bound together and thus represents a worst case challenge air removal. In its simplest form, the test pack contains at its centre a piece of paper with a diagonal cross of autoclave indicator tape placed on it. The pack is subjected to the routine autoclave cycle and the tape cross is examined for any unevenness in colour, which indicates incomplete air removal. For qualification purposes the test can be made quantitative by placing thermocouples at the centre of the pack and on the exterior and comparing temperature difference – any depression of temperature at the centre of the pack indicates incomplete air removal. The Bowie-Dick tape test or equivalent (AMSCO DART, Lantor cube, Brown's TST pack) is typically used once a week in an empty chamber to confirm air removal capability.

Finally, it is common practice in the United Kingdom and Ireland to carry out a chamber leak rate test at the beginning of each day, using an empty, dry, warm autoclave chamber. The chamber is evacuated and then isolated by closing all valves. The ability of the isolated chamber to hold that vacuum is then assessed. A pressure rise of not more than 13mbar in 10 minutes is considered acceptable (see EN285). A greater rise indicates a leak on the chamber, for example due to a faulty door seal, which could permit entry of air to the chamber during the pre-sterilisation phase of the cycle.

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STEAM QUALITY

If we are to take such elaborate measures to ensure air removal from our loads, it follows that the steam we introduce should not contain air. This is why EN285 contains a test for **non-condensable gases** in steam. The percentage of such gases (usually air) should not exceed 3.5%.

SO MUCH FOR THE THEORY – IS THERE A PROBLEM IN PRACTICE?

Many industry representatives (and some regulators) view the concern placed on air removal by European (particularly United Kingdom and Irish) regulators as excessive. Is this just a solution in search of a problem or is there a real problem?

Last year we visited a company in North America manufacturing aseptically prepared products. The company had experienced several media fill failures, which it attributed to media contamination. The autoclave cycle used to sterilise the filter and stoppers consisted of a single vacuum pulse to remove air. The cycle had been validated using bio-indicators, but no air removal tests had ever been performed on the autoclave.

Review of the validation data showed that some thermocouples achieved sterilising temperature over 4 minutes later than the majority, indicating to us a potential air removal problem. We encouraged the company to put a Bowie-Dick test pack into the autoclave and run the same cycle – it failed catastrophically! We then encouraged the company to incorporate a series of negative and positive pulses into the pre-sterilisation phase of the cycle. After doing so…

- all Bowie-Dick tests passed
- all thermocouples in validation studies reached 121°c within 30 seconds
- all subsequent media fills passed.

FURTHER READING

EN285, "Sterilisation – Steam Sterilisers"

Health Technical Memorandum 2010, "Sterilisation", HMSO, London

For more information, contact **pharmamail@nsf.org** or visit **www.nsfpharmabiotech.org**

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