END OF SESSION BROTH FILL TECHNIQUE FOR STERILITY ASSURANCE OF PRODUCTS ASEPTICALLY PREPARED IN SECTION 10 UNITS

1st Edition

April 2007

END OF SESSION BROTH FILL TECHNIQUE FOR STERILITY ASSURANCE OF PRODUCTS ASEPTICALLY PREPARED IN SECTION 10 UNITS

Introduction

The way in which sterility is assured for aseptically prepared products in Section 10 hospital units is varied. This may involve aliquots of products taken for sterility testing, additional samples made for sterility testing, unused products or end of session broth fill techniques utilising used or fresh components from the session or a lack of product testing entirely.

Such methods are in addition to all the assurance and GMP procedures inherent in operating a successful aseptic preparation service.

Aim

The aim of this paper is to promote the end of session broth fill technique as the method of choice for sterility assurance in Section 10 units.

Existing advice

Aseptic Dispensing for NHS Patients (DoH 1995, Farwell J) recommends that "Sampling from final containers should be avoided unless the product is surplus to requirements. Samples may be taken at the end of the compounding operation before final seals are in place. They may be used to confirm accurately the chemical composition of solutions but there is limited value in testing them microbiologically unless the whole volume in the container is used. Further sampling of the final container is another threat to the integrity of the product and if undertaken would need to be incorporated in the validation system. The test for sterility is an important test not only for validation purposes but also for routine control. A sampling scheme should be in place such that extra containers are prepared on a routine basis and subjected to a validated test for sterility. The test should as far as reasonably practicable follow the requirements of the British Pharmacopoeia."

The Quality Assurance of Aseptic Preparation Services (Ed A M Beaney, 4th edition 2006) recommends "There should be a planned programme of physical, chemical and microbiological analysis of the finished product as appropriate. Samples may be obtained from unused products, extra specially prepared samples, an in-process sample taken at the end of the compounding procedure before the final seals are in place and before removal from the critical zone".

End of session broth fill technique – practicalities

This method involves using a nutrient media, typically Tryptone Soy Broth, to rinse through a range of components and containers which have been used for the preparation of product(s). If it is likely that product residues within the components would inhibit growth then the use of fresh components is permitted. It is carried out at the end of a working session once all production has been completed and product removed from the critical area, but before the critical area has been cleaned. It is carried out by the operator who prepared the products during the session. The exact method will need to be adapted to each aseptic unit to reflect individual practices. Examples of the technique include:-

- Running media through PN compounding lines and other access devices
- Filling used containers with media
- Filling syringes that have been used for additives

A suggested minimum frequency of applying the technique is one end of session broth fill per process (e.g. PN, CIVA, CYTO product) per week, to be rotated through the operators.

The filled broth units are incubated for 14 days (7 days at 20-25^{o}C followed by 7 days at 30-35^{o}C) without any further manipulation. Results are reported to the responsible pharmacist or their deputy.

If an end of session broth fill exhibits growth then this needs to be followed up by actions which can include the following:

- Quarantine any unused product from the session, which can be used for further testing.
- Increase the end of session broth fill test frequency.
- Investigate the possible causes e.g. Reviewing training, equipment, aseptic process, aseptic transfer.

It is important to validate the process to ensure that traces of residual product would not impede growth. This may be carried out by a post incubation media fertility check using an inoculation of micro-organisms as described in A1.7.3, the Quality Assurance of Aseptic Preparation Services (Ed A M Beaney, 4th edition 2006)

Summary

The main advantage of using this technique is that any microbial growth observed in the end of session broth fill units can only have originated in the aseptic production unit and is directly related to the items used, the equipment or the process and environment. The use of the end of session broth fill test will reduce the frequency of sterility testing for a range of products and replace it with a timely and more robust method of assessment.

Prepared by Trevor Munton and the Microbiology Protocols Group, a working group of the NHS Pharmaceutical Quality Assurance Committee.

April 2007

Members of the Microbiology Protocols Group

Trevor Munton
Phil Hunt
John Rhodes
Alison Webber