

'Implementation of BacT/ALERT (Biomerieux®) culture bottles in a hospital pharmacy production unit for the sterility testing of chemotherapeutic batches'

BACKGROUND

Due to an increase in production of chemotherapeutics, we implemented dosebanding of chemotherapeutic drugs to prevent errors and improve the quality of the cytotoxic drug preparation. The standard sterility tests who are recommended by the European Pharmacopeia on chemotherapeutic batches are time-consuming (14 days incubation before final result).

PURPOSE

The goal of the study is to create a more sensitive sterility test, which assures us a more quick and reliable result which minors the period of quarantine of chemotherapeutic infusions from that batch.

METHODS

We investigated the BacT/ALERT® (BioMérieux) culture bottles as a rapid microbiological method. Microbiological growth creates CO₂ production which is detected by an automatic photometric method.

Many types of BacT/ALERT® culture bottles are available, we selected the FA culture bottles (ref.410851). These culture bottles are excellent for the detection of aerobic and facultative anaerobic microorganisms (bacteria and fungi), which are the most commonly found microorganisms in a hospital pharmacy production unit.

We inoculated the bottles with one of the four standard microorganisms which are recommended in the European Pharmacopeia. We added each time 10-100 colony-forming units of *Staphylococcus aureus* (SA, ATCC6538), *Pseudomonas aeruginosa* (PA, ATCC9027), *Bacillus subtilis* (BS, ATCC6633) or *Candida albicans* (CA, ATCC10231).

We compared every step with a traditional tryptic soy broth (BioMérieux, ref.42633) with a phased incubation period (14 days) as recommended by the PIC/s, WHO, etc. .



Table 1. Influence on the growth of micro-organisms in a standard TSB medium and a BacT/Alert culture bottle.
Legend: -: no growth, +: growth and d: days

Micro-organism	TSB	Bact/Alert FA
Negative control	-	-
<i>Pseudomonas aeruginosa</i>	+ (<3 d)	+ (0,58 d)
<i>Staphylococcus aureus</i>	+ (<3 d)	+ (0,53 d)
<i>Bacillus subtilis</i>	+ (<3 d)	+ (0,45 d)
<i>Candida albicans</i>	+ (<3 d)	+ (1,97 d)

In chemotherapeutic batch production, it is important to take the possible inhibition of microorganism growth by the cytotoxic drugs in account. We tested the bacterial growth with the highest cytotoxic batch-concentration, 0,4 mg/ml for paclitaxel and 1,9 mg/ml for trastuzumab.

Table 2. Influence of a chemotherapeuticum on the growth of micro-organisms in a standard TSB medium and a BacT/Alert culture bottle.
Legend: -: no growth, +: growth and d: days

Micro-organism	Paclitaxel (0,4 mg/ml)		Trastuzumab (1,9 mg/ml)	
	BACT/Alert	TSB	Bact/Alert	TSB
Negative control	-	-	-	-
<i>Pseudomonas aeruginosa</i>	+ (2,37 d)	+ (<5 d)	+ (0,55 d)	+ (<3 d)
<i>Staphylococcus aureus</i>	+ (0,75 d)	+ (<5 d)	+ (0,58 d)	+ (<3 d)
<i>Bacillus subtilis</i>	+ (0,62 d)	+ (<5 d)	+ (0,43 d)	+ (<3 d)
<i>Candida albicans</i>	+ (3,28 d)	+ (<5 d)	+ (2,01 d)	+ (<5 d)

RESULTS AND DISCUSSION

All micro-organisms were detected in both techniques, but the BacT/Alert® method gives a faster result. Part in detection but also in perception, the electronic message will inform you if there is a positive result and you can participate in a timely manner. By the automatic photometric method is the risk of false positive or false negative results (false visual observation) non-existent.

The influence of the chemotherapeutic drug is dependent on the structure/toxicity of the drug. Trastuzumab, which is a protein will do no harm to the present micro-organism. This is shown in the detection-time where there is no difference with or without trastuzumab, which concludes that trastuzumab has no toxicity on bacteria and yeasts.

Paclitaxel however, shows us an inhibition effect with all the tested micro-organisms but especially with *Pseudomonas aeruginosa* and *Candida albicans*. Further research has to define the effect of paclitaxel on these two strains.

After evaluating the results we programmed the BacT/Alert® device to incubate and screen the culture bottles for 7 days, which is still faster than the standardized method (PIC/s...). The above results indicate also that the detection of all growth has been observed before 4 days.

We can still say that the BacT/Alert® method is much more efficient in detection and will give us an earlier result when there is a contamination. The rapid microbiological test led us to a trusted system of early release in chemotherapeutic infusions of a batch.

CONCLUSION

- BacT/ALERT® culture bottles can successfully be implemented in a hospital pharmacy production unit. Our goal to install a more sensitive and rapid detection method for sterility testing could be achieved and led to a more secure system in the release of chemotherapeutic infusions.
- Further research with other cytotoxic drugs will be needed to validate this method.