Cold Filterable Tryptone Soya Broth: CM1065

A gamma-irradiated, cold filterable Tryptone Soya Broth (cfTSB) suitable for microbiological Media Fill Trials (MFT) for the pharmaceutical industry.

NUTRITIOUS

Cold Filterable Tryptone Soya Broth is a highly nutritious, general purpose medium which supports the growth of a wide range of bacteria, yeasts and moulds[1].

RECOMMENDED

The formulation of cfTSB conforms to the European Pharmacopoeia 6th Edition 2008[2], the British Pharmacopoeia 2003[3], the US Pharmacopoeia 30 NF22 2008[4] and the Japanese Pharmacopoeia XV 2006[5].

EASY TO USE

Each component of cfTSB has been specially screened and selected to ensure easy filtration. Filtration performance (V_{cap}) is determined with three different filter types for every batch.

CONVENIENT

Packs of cfTSB have been given a sterilising dose of gamma-irradiation (minimum 25 kGy) validated to be lethal for all yeasts, moulds and bacteria including bacterial spores and mycoplasmas.

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Intended Use

This medium is particularly suitable for use in pharmaceutical Media Fill Trials (MFT). Dehydrated cfTSB can be substituted for the powdered components that go into making aqueous injectable drugs or added as a sterile liquid downstream of processing a placebo for solid dosage form. After carrying out MFT, the medium is incubated under appropriate conditions for the recovery of any bacteria, yeasts and moulds.

Principles

Oxoid pre-screen and select the raw materials that go into cfTSB so that every batch of product will have a high V_{cap} value. V_{cap} is the theoretical maximum volumetric throughput for the filter under test. With this information, the maximum filterable volume of TSB may be calculated before starting a MFT[7].

At Oxoid, a filter management system is used with a test filters to determine V_{cap} values for each batch of cfTSB. The final filterable volume of TSB will depend on the membrane type, pore size and area of the process filter used. Each batch of Oxoid cfTSB will have a minimum V_{cap} of 2,800 litres/m^2 for the three filter types tested (0.2µm pore size).

Typical V_{cap} values for Oxoid cfTSB:

Filter membrane	V_{cap} (ml) 47mm disc (area 14cm^2)	V_{cap} (litres/m^2)
Polyvinylidene fluoride (PVDF)	4,909	3,506
Polyethersulfone (PES)	6,700	4,786
Nylon (NR)	4,561	3,258

Vcap is the extrapolation to a "flow = zero" point; the time to this point may be very long. Therefore, V_{cap} is good for comparative analysis but is not practical for MFT where time for a process is limited. A more useful value is V_{90}, which is calculated as 68% of V_{cap} and is the point at which flow has decayed to 10% of the initial rate[7]. Contact your filter manufacturer for guidance.

N.B. cfTSB should not be used to validate the suitability of the chosen filtration system for its ability to provide a sterile drug product. The components of TSB will be quite different to those found in an aqueous drug formulation, and validation for this purpose should be carried out on the drug preparation itself.

Summary

'Sterile for use' liquid drugs often contain heat-sensitive components which mean that terminal sterilisation by autoclaving is not an option. Sterilisation by filtering (for soluble liquids) followed by filling under aseptic conditions is the method for preparation of these types of drug. The purpose of MFT is to provide a measure of the likelihood of microbiological contamination arising in a particular aseptic process. Typically, the composition of a liquid injectable drug means that that a very large volume can be filtered before blocking of that filter occurs. Due to the biological nature of TSB, filters will block sooner which will mean that the medium will have to be heated or filters changed during a MFT.

Formula

cfTSB (CM1065)

	Grams per litre
Pancreatic digest of casein	17.0
Papaic digest of soybean meal	3.0
Sodium chloride	5.0
Di-potassium hydrogen phosphate	2.5
Glucose	2.5
Final pH 7.3 ± 0.2 at 25°C	

Directions

Add 30g of cfTSB to 1 litre of distilled water. Mix well to dissolve completely. Sterilise by filtration or by autoclaving at 121°C for 15 minutes.

Incubation of MFT units is usually carried out for 14 days[6] at both 20-25°C and 30-35°C. Where possible, visual inspection of the units should be carried out on a daily or every second day basis. Micro-organisms from any contaminated units should be subcultured, purified and identified to species level. Refer to the appropriate regulatory body for full guidelines[2,3,4,5].

Appearance

Dehydrated medium: straw coloured, free-flowing powder
Prepared medium: straw coloured solution

Precautions

Do not use beyond the stated expiry date, or if the product shows any sign of deterioration.

Storage and Stability

Dehydrated cfTSB must be stored tightly capped in the original container at 10-30°C. When stored as directed, the unopened product will remain stable until the expiry date printed on the container.

Material Safety Data Sheet (MSDS) and Batch Quality Control Certificates are available from the Oxoid website: www.oxoid.com.

Quality Control Testing

Organism	Culti-Loops™ order code	Typical appearance
Staphylococcus aureus ATCC®6538™†	C7016L	Turbid growth
Pseudomonas aeruginosa ATCC®9027™†	C5210L	Turbid growth
Bacillus subtilis ATCC®6633™†	C1221L	Flocculent/surface growth
Aspergillus brasiliensis ATCC®16404™†	C1100L	White mycelia, black spores or no spores
Candida albicans ATCC®10231™†	C1503L	Flocculent/surface growth
Un-inoculated medium	N/A	No growth

References

1. Oxoid Manual 8th Edition, 1998, p2-208 2. European Pharmacopoeia 6th Edition 2008 3. British Pharmacopoeia 2008 4. US Pharmacopoeia 30 NF22 2008 5. Japanese Pharmacopoeia XV 2006 6. Microbiological Media Fills Explained by Nigel Halls, 2002. Sue Horwood Publishing Ltd., UK. 7. Badmington, F., Wilkins, R., Payne, M. and Honig, E.S. Vmax Testing for Practical Microfiltration Train Scale-Up in Biopharmaceutical Processing *Pharmaceutical Technology* September 1995 p64-76

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