

ISO 13485; CE CERTIFIED; USDA/AUSTRALIAN
EDQM CERTIFIED

FOETAL BOVINE SERUM

SERA



Introduction

Serum is commonly used as a supplement to basal growth medium in cell culture. The most common type of serum used for cell growth is foetal bovine serum (FBS), also known as foetal calf serum (FCS).

Foetal bovine serum is obtained from foetuses harvested in abattoirs from healthy dams fit for human consumption.

Occasionally, there may be use of other bovine sera, such as newborn calf serum or donor bovine serum. In cell culture, serum provides a wide variety of macromolecular proteins, low molecular weight nutrients, carrier proteins for water - insoluble components, and other compounds necessary for in vitro growth of cells, such as hormones and attachment factors. Serum also adds buffering capacity to the medium and binds or neutralizes toxic components. Attempts to replace serum entirely with serum-free medium have met only with limited success.

The selection of a serum supplement for cell culture applications is primarily dependent on the chemical definition of the basal medium, the type of cell to be grown, and the culture system being employed.

Collection

In the FBS manufacturing process, whole blood is collected aseptically in disposable sterile plastic bags and allowed to clot. Once the serum has been separated from the clot, it is pooled and frozen.

Controlling the initial collection of foetal blood is a crucial factor in the quality of the final serum product. Only raw material that meets our specifications is approved for production.

Handling Serum Products

Using Serum - Although the product has been sterile filtered, aseptic procedures must be followed at all times.

Granules, flocculent material or turbidity may develop after thawing. This particulate matter does not alter the performance of the serum as a supplement for cell culture medium. Repeated freezing/thawing of serum may increase the amount of precipitate and is therefore not recommended. If you do not intend to use an entire bottle of serum aliquot it into usable quantities in sterile containers before freezing a second time.

Wipe the outside of each bottle with a suitable disinfectant solution, before setting it on the work surface. Remove the heat seal and wipe the outside of the cap with the disinfectant solution.

All serum products should be treated as potentially harmful and appropriate care should be taken when handling them.

Raw Materials

Two distinct grades of FBS are available on the world market: USDA-Grade FBS and European-Grade FBS.

USDA-Grade FBS is produced from raw materials originating only from countries certified to be free of both BSE (Bovine Spongiform Encephalopathy) and FMD (Foot and Mouth Disease). This product can be freely imported into any country, and is the product of choice in all countries for manufacturing purposes. Furthermore, only the use of this product allows researchers to send their cells, or the products of their cells, to collaborators in other countries with strict import regulations.

All FBS processed in the Biological Industries plant is USDA-Grade.

Processing

Selected batches of serum raw material are thawed, tested for endotoxins and hemoglobin content and only the accepted material is pooled. The pooled raw material is thoroughly blended under refrigerated conditions and membrane filtered for sterility according to a well validated filtration protocol. Biological Industries processes FBS through a sequence of pre-filters and membrane filters. The filtration step includes the use of three 0.1 micron sterilizing grade membrane filters in series.

After filtration, the serum is dispensed into bottles by an aseptic filling process which has been validated to insure sterility of the final product. Serum products are produced in a controlled environment (clean rooms) designed to carefully control air pressure and particulate matter.

The manufacturing area is a class 100,000 (ISO 8) environment. The sterile bottles and equipment are stored in a class 10,000 (ISO 7) environment, and the filling room is a class 1000 (ISO 6) environment with class 100 (ISO 5) laminar air flow sterile bench.

Clean rooms are monitored on a regular basis for particulate and microbial levels to ensure that the air handling system, cleaning protocols and personnel maintain standards control.

After filling, the final product is quickly frozen to -20°C and held in quarantine until all quality control tests have been completed.

Quality Control

Each lot of FBS is tested to confirm that the serum meets the written specifications. Final product release is done after reviewing all production and quality control records to determine compliance with all established, approved written procedures.

Physical and chemical tests

- Electrophoretic Pattern
- pH
- Osmolality



- Total proteins
- Albumin
- IgG
- Hemoglobin
- Globulins

Biochemicals Tests

The following tests are conducted on each lot of FBS:

- Alanine Transaminase (ALT)
- Alkaline Phosphatase
- Aspartate Aminotransferase (ast)
- Bilirubin - total
- Bilirubin - direct
- Blood Urea Nitrogen (BUN)
- Calcium
- Chloride
- Cholesterol
- Creatinine
- Creatinine Kinase (CK)
- Gamma-Glutamyl Transferase (GGT)
- Glucose
- High Density Lipoproteins (HDL)
- Lactate Dehydrogenase
- Low density Lipoproteins (LDL)
- Phosphorous (Inorganic)
- Potassium
- Sodium
- Triglycerides (TG)
- Uric Acid

Microbiological tests

- Sterility tests:
Bacterial and fungal sterility tests according to the current USP
- Mycoplasma contamination:
According to the Code of Federal Regulations (CFR), title 9, part 113 (culture method).
- Viral contaminants:
According to the protocols described in CFR, title 9, part 113 for Bovine Viral Diarrhea (BVD), Infectious Bovine Rhinotracheitis (IBR) and Parainfluenza type 3 (PI3).
- Viral antibodies:
FBS is screened to determine the titer of neutralizing antibodies to BVD, IBR and PI3.

- Endotoxins:
The test is performed using the standard Limulus Amebocyte Lysate (LAL) with the kinetic turbidimetric method.

Biological performance (cell growth)

The cell growth tests are designed to check the efficacy of the FBS in promoting cell growth. Cells used are fibroblasts (MRC-5 diploid normal cells), epithelial cells Vero and hybridoma cells. Each test is conducted using the tested serum and a validated control lot. Growth promotion using MRC-5 cells is evaluated through several subculture generations to observe any evidence of cytotoxicity and morphological changes of the cells. Vero cells (ATCC, CCL 81): plating efficiency.

MRC-5 cells (ATCC, CCL 171): 3 passages test.

Hybridoma cells: cell growth.

Stability

FBS stability at -20°C temperature was evaluated with several cell types for long periods. The FBS did not lose its performance for 55 months (4.5 years) with all the cells tested. Storage of FBS at -20°C without defrosting will maintain the quality of the FBS at least until the expiration date stated on the label.

Quality Assurance

The FBS production process is carried out under controlled conditions in a controlled environment. The steam-in-place (SIP) sterilization, filtration for sterility and filling are validated as required for key aseptic processes. A dossier (Device Master Record) exists for serum with all relevant data concerning serum production. The production process from the raw material to the final product in storage, as well as the quality control tests and results, are documented and filed to ensure traceability and control of the process.

Biological Industries' products are manufactured in compliance with the quality management standard ISO 9001:2000 and ISO 13485:2003. Certifications are available upon request.

In addition, the FBS production process conforms to the In Vitro Diagnostics Directive (IVDD 78/79/EC) of the European Parliament. Therefore, our FBS received the CE mark making it eligible for sale in the European Union for in vitro diagnostics.

A Bovine Spongiform Encephalopathy (BSE) Certificate of Suitability has been issued to Biological Industries by the European Directorate for the Quality of Medicines (EDQM) in accordance with monographs of the European Pharmacopoeia.

All documents and certifications are available upon request.



Foetal Bovine Sera (FBS)

Serum, as a biological material, represents an undefined mixture of components in which composition varies from one lot to the other. Some cell types are sensitive to the variations in serum performance. Customers are encouraged to evaluate serum samples with their own culture system and cells while we reserve the quantities of the specific lots until customer testing is completed. In this way, the customer may choose the best serum for his own applications.

Biological Industries offers you the following certified sterile Foetal Bovine Serum Products:

Product Name	Catalogue No.	Unit Size	Storage Temp.
Certified Foetal Bovine Serum	04-001-1A	500ml	-20°C
	04-001-1B	100ml	-20°C
Certified Foetal Bovine Serum Heat Inactivated	04-121-1A	500ml	-20°C
	04-121-1B	100ml	-20°C
Certified Foetal Bovine Serum Qualified for Human Embryonic Stem Cells	04-002-1A	500ml	-20°C
	04-002-1B	100ml	-20°C
Certified Foetal Bovine Serum Qualified for Human Embryonic Stem Cells Heat Inactivated	04-222-1A	500ml	-20°C
	04-222-1B	100ml	-20°C
Certified Foetal Bovine Serum Functionally Tested for use with Tetracycline Regulated Systems	04-005-1A	500ml	-20°C
	04-005-1B	100ml	-20°C
Certified Foetal Bovine Serum Functionally Tested for use with Tetracycline Regulated Systems Heat Inactivated	04-125-1A	500ml	-20°C
	04-125-1B	100ml	-20°C
Certified Foetal Bovine Serum Dialyzed	04-011-1A	500ml	-20°C
	04-011-1B	100ml	-20°C
Certified Foetal Bovine Serum Charcoal-Stripped	04-201-1A	500ml	-20°C
	04-201-1B	100ml	-20°C

European Grade Approved FBS:

Product Name	Catalogue No.	Unit Size	Storage Temp.
Foetal Bovine Serum (FBS) European Grade	04-007-1A	500ml	-20°C
	04-007-1B	100ml	-20°C
Foetal Bovine Serum (FBS) European Grade Heat Inactivated	04-127-1A	500ml	-20°C
	04-127-1B	100ml	-20°C

Heat inactivated FBS

Product Name	Catalogue No.	Unit Size	Storage Temp.
Certified Foetal Bovine Serum Heat Inactivated	04-121-1A	500ml	-20°C
	04-121-1B	100ml	-20°C

Heat inactivation of serum is performed by raising the temperature of the serum to 56°C and maintaining that temperature for 30 minutes. Heat inactivation is the method of choice to destroy complement proteins activity.

