

# PRODUCT DATA SHEET

## Specialty Fetal Bovine Serum

### Description

#### *Heat Inactivated*

All of the Atlanta Biologicals fetal bovine serum (FBS) products are available in the heat inactivated form. The most common objective of heat inactivation is to destroy heat-labile components such as complement that may adversely affect the growth performance of some cell cultures. Serum is inactivated by raising the temperature to 56°C for 30 minutes under controlled conditions.

#### *Embryonic Stem Cell Qualified*

For applications that utilize embryonic stem cells, the success of the research is dependent on using an FBS lot that has been qualified for the culture of this cell line. The Embryonic Stem Cell Qualified FBS offered by Atlanta Biologicals has eliminated the time-consuming process of pre-screening multiple serum lots. High quality FBS is screened for plating efficiency, colony morphology and cytotoxicity to identify lots that are particularly suited for the culture of embryonic stem cells. Embryonic Stem Cell Qualified lots must show outstanding performance, while maintaining the cells in their undifferentiated state.

#### *Hybridoma Qualified*

Hybridoma Qualified serum is suited for the culture of hybridoma and myeloma cell lines. High quality FBS is screened to identify lots that offer optimal performance with these cell lines. Hybridoma Qualified lots must show superior growth promotion, exceptional clonal growth at limiting dilution and a lack of cytotoxicity during the growth studies.

#### *Insect Cell Qualified*

Insect Cell Qualified serum is suited for the culture of insect cell lines. High quality FBS is screened for optimal performance with these cell lines. Insect Cell Qualified lots demonstrate superior cell yield, exceptional viability and a lack of cytotoxicity in cell culture systems.

#### *TET Tested*

The Tet systems are the most widely applied inducible gene expression system. In each system, a tetracycline-controlled transactivator interacts with a responsive promoter to regulate expression of the gene of interest. The expression is controlled from outside by tetracycline or one of its derivatives, known as effector substances. The presence of the effector substances in serum may interfere with the tetracycline-regulated gene expression systems. TET Tested serum is specifically qualified for use in Tet systems and cell lines. The tetracycline and tetracycline derivative levels in high quality FBS are measured and those lots with undetectable levels are selected as TET Tested FBS.

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### *Charcoal/Dextran Treated*

Charcoal/Dextran treated FBS is used in applications that require lower levels of hormones, steroids and growth factors such as insulin and estrogen related research. Pre-selected, high quality FBS is processed using a proprietary Charcoal/Dextran treatment that has been shown to reduce the levels of many hormones, steroids and growth factors. Each lot of serum is tested for the hormone and steroid levels before and after treatment to confirm the efficacy of the process.

### *Dialyzed*

Dialyzed FBS is used in cell culture systems requiring a more defined environment of small molecules. Dialysis reduces the concentration of low molecular weight components such as nucleotides, amino acids, hormones, salts and various small proteins. The serum is dialyzed against physiological saline using a 10,000 Dalton or a 12,000 to 14,000 Dalton cutoff membrane. The process is controlled by monitoring the glucose concentration during the procedure. In order to prevent precipitation and inactivation of serum peptides, exhaustive dialysis is not performed.

### *Gamma Irradiated*

Even though FBS is stringently tested, common bovine viruses may exist in levels that are below the detection limits of current test methods. Gamma irradiation is recognized as an effective method for inactivating viruses and other adventitious agents found in FBS. The gamma irradiated FBS is exposed to a Cobalt 60 source at a delivered dose of 25-35 kGy. Exposure to this dosage has been shown to remove up to 6 logs of many extraneous agents, while preserving the growth performance characteristics of the serum.

## **Collection and Processing**

Atlanta Biologicals consistently supplies FBS lots with excellent cell growth characteristics, low endotoxin and low hemoglobin values. Our sera are produced by maintaining direct control over every process step from the initial raw material processing at the collection sites, to final filtration, bottling and quality control. This vertical integration allows Atlanta Biologicals to assure production of high quality sera and to minimize lot-to-lot variation.

### *Origin:*

The FBS used in Atlanta Biologicals' manufacturing process meets all of the USDA requirements for animal products. All of our FBS is traceable back to the date and location of collection. The USDA restricts importation of serum from areas that are considered to have or are at high risk for exotic diseases, including foot and mouth disease (FMD) and bovine spongiform encephalopathy (BSE). In addition, all of Atlanta Biologicals' serum used in manufacturing must meet our strict quality requirements for raw material.

### *Closed System Collection:*

Since the beginning of mammalian cell culture back in the 1950s, there has been a constant demand for high quality FBS used to support the growth of cells *in vitro*. Our customers' need for quality and consistency has led Atlanta Biologicals to create an extensive network of serum collection sites for FBS. Atlanta Biologicals' direct control over the serum collection sites and our pioneering collection

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techniques have resulted in a stable, traceable supply of quality serum for our customers. This network continues to grow even today, allowing us to consistently meet our customers' needs, even as the global supply of FBS fluctuates due to environmental factors such as regional droughts, natural disasters, disease outbreaks and other circumstances that affect our industry.

The quality of FBS is determined primarily at the blood collection site and in the initial serum processing. Atlanta Biologicals closely monitors each step of the production process at these critical stages to assure that the raw material meets our highest quality standards. The bovine blood is collected using a closed loop system that minimizes bacterial contamination during collection and yields serum with low levels of endotoxin. To reduce hemolysis and improve product quality, the whole blood is kept at refrigerated temperatures from the time of collection until it is processed.

### *Raw Material Processing:*

The whole blood is allowed to clot at refrigerated temperatures. Serum is then carefully removed from the clot after centrifugation at refrigerated temperatures, to avoid contamination by red blood cells. This raw serum product is immediately placed into bottles and frozen for delivery to our manufacturing facility. The product remains frozen throughout the entire shipping and receiving process, from the raw processing site to our manufacturing facility. This rapid processing ensures that endotoxin levels in the serum remain low and that the growth promoting qualities of the serum remain at their peak levels.

### *Filtration:*

Approved lots of raw serum are thawed under controlled conditions and sterile filtered by an in-line process that uses multiple 0.1µm filters for the final filtration step. Filling takes place in a laminar flow hood certified to maintain Class 100 conditions. The filling room is maintained under positive pressure with HEPA-filtered air. The serum is aseptically dispensed into gamma irradiated, sterile PETG or PETE bottles. Filled containers are immediately labeled and frozen, and then maintained at temperatures less than -5°C to preserve the product quality.

## Quality Control Testing

### *Chemical Analyses: (All FBS grades)*

The Osmolality (vapor pressure method) and pH are measured on instruments that are calibrated daily using reference solutions traceable to National Institute of Standards and Technology Reference Materials.

Hemoglobin content of the serum is measured spectrophotometrically.

Endotoxin content is measured using the Limulus amoebocyte lysate (LAL) gel-clotting assay.

### *Biochemical Profile: (All FBS grades - different FBS grades may vary from the profile shown)*

Total Protein	Total Bilirubin	Blood Urea Nitrogen (BUN)	Sodium/Potassium Ratio
Albumin	Iron	Creatinine	Chloride
Globulin	UIBC	BUN/Creatinine Ratio	Calcium
A/G ratio	Cholesterol	Uric Acid	Phosphorus
IgG	Triglycerides	Sodium	Magnesium
ALT/SGPT	Glucose	Potassium	Bicarbonate
Alkaline Phosphatase			

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**Microbiological Testing:** (All FBS grades)

Each lot of serum is tested to confirm the absence of bacterial or fungal contamination using modified methods referenced in the U.S. Pharmacopeia (USP).

Each lot of serum is tested to confirm the absence of mycoplasma contamination to the limit of detection with the methods used. The large-volume method of Barile and Kern is used to detect mycoplasma that can be cultivated in media. Three different media are inoculated with the serum sample and grown under both aerobic and anaerobic conditions. Non-cultivable mycoplasma are detected by passage of the sample on an indicator cell line and staining with a DNA-fluorochrome.

**Virus Testing:** (All FBS grades)

Serum is tested for adventitious agents using modified procedures adapted from the Code of Federal Regulations, Title 9, Section 113.53, "Requirements for Ingredients of Animal Origin". Virus susceptible cell cultures previously shown to be free of viral contamination are cultured in medium containing the test serum. During this period, cultures are examined microscopically for evidence of virus-induced morphological changes or cytopathogenic effects. After multiple passages and a minimum of 21 days, the cultures are tested for the presence of specific viral agents (see chart below) by fluorescent antibody staining, for cytopathogenic viral agents such as Infectious Bovine Rhinotracheitis virus (IBRV) by geimsa staining and for hemadsorbing viral agents such as Parainfluenza-3 virus (PI-3V).

## Storage and Handling

The specialty FBS is supplied in gamma irradiated, sterile PETG or PETE bottles. We recommend that the serum be stored frozen at a temperature of -5°C to -20°C. Multiple freeze-thaw cycles of the serum should be avoided as this may lead to deterioration of the product. If intermittent usage of the product is anticipated, we recommend use of either our smaller package sizes or dividing the serum into smaller aliquots suitable for single use. Always use aseptic techniques when handling the serum and aliquot into sterile containers.

## Shipping

Serum is shipped frozen by next day air in insulated containers packed with dry ice.

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