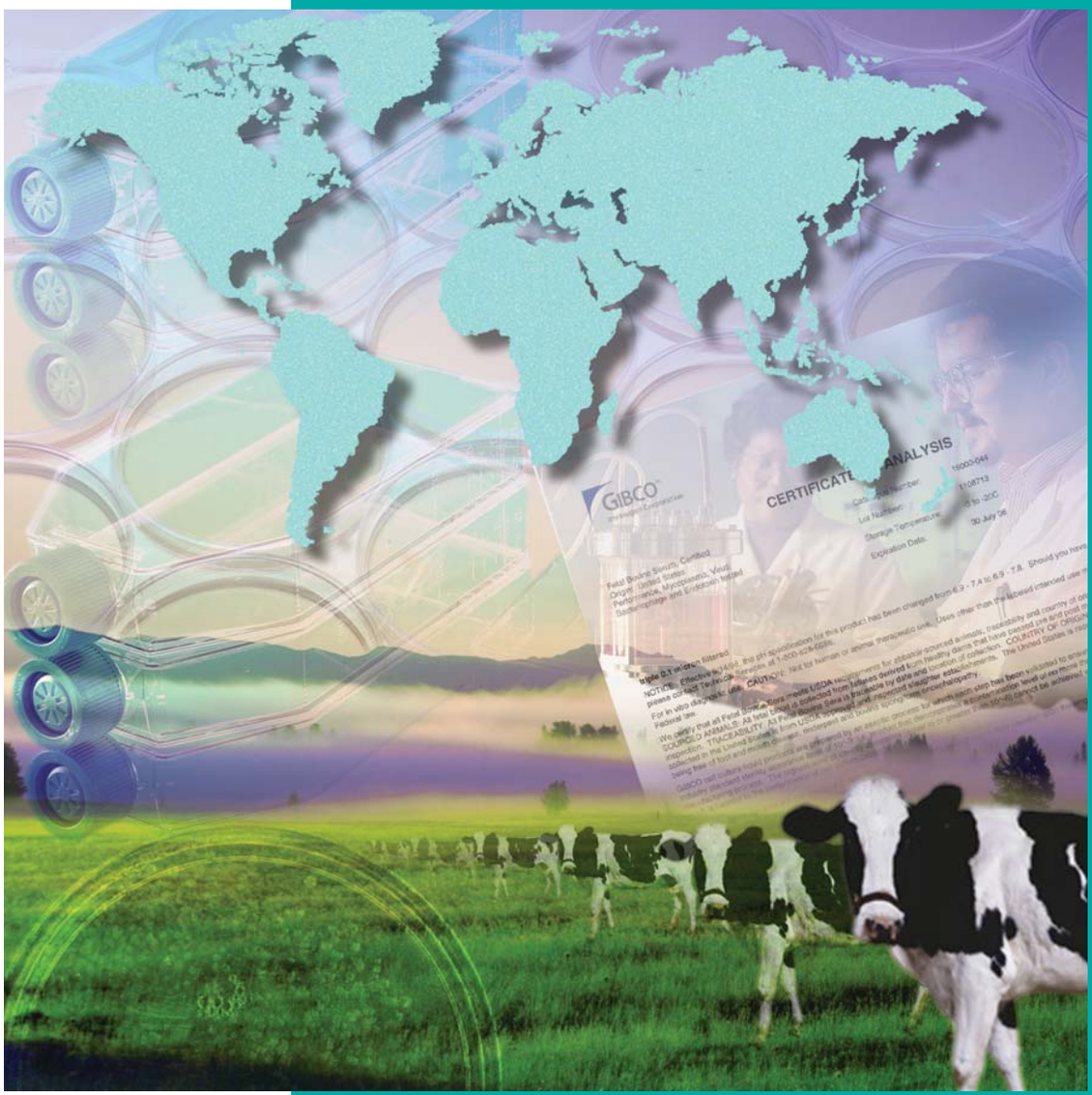
Fetal Bovine Serum



Gibco®
invitrogen cell culture

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Consider the source.

For over 40 years, Gibco® brand cell culture products have set the global standard. We ensure that your FBS is the best available by sourcing serum only from countries that meet the strict import requirements of the United States Department of Agriculture (USDA).

All lots of Gibco® FBS:

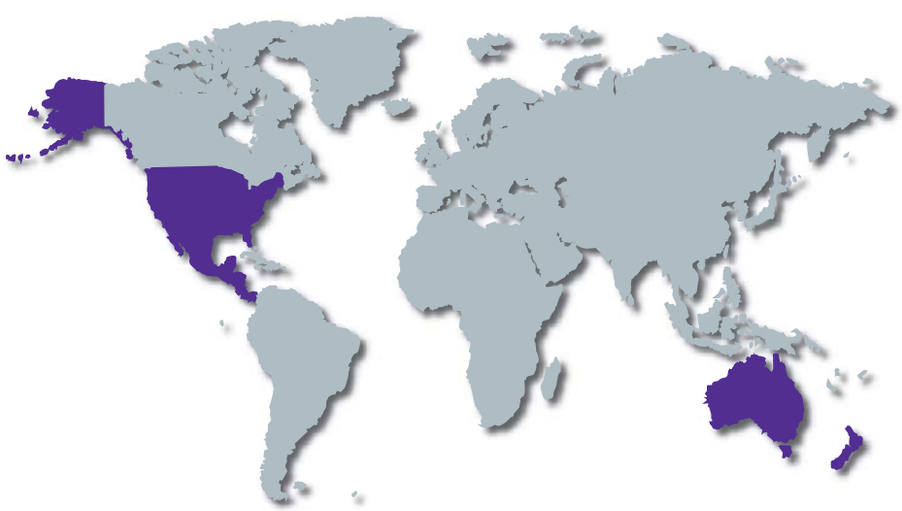
- Pass stringent quality control tests
- Are never blended with FBS from other locations
- Meet strict importation requirements
- Are shipped with a Certificate of Analysis that identifies the country of origin

As a by-product of the beef and dairy industries, FBS is affected by factors as complex and varied as health concerns and market conditions.

One of the world's largest suppliers of FBS, Invitrogen obtains serum only from countries recognized by the United States Department of Agriculture (USDA) as being free of foot and mouth disease, rinderpest, and bovine spongiform encephalopathy (BSE). These include the United States*, Australia, Mexico, Central America and New Zealand. Since there is a finite amount of serum available from any one source, we source from them all.

The selling price of FBS is dictated by its country of origin and is influenced by supply and demand. By obtaining sera from multiple locations, we can offer a selection of high-quality Gibco® FBS, allowing you to decide which is the best value for your requirements.

When you rely on us, you have choices. And an uninterrupted supply of FBS.



One of the world's largest suppliers of fetal bovine serum (FBS), we obtain serum from the United States and other countries recognized by the United States Department of Agriculture (USDA) as being free of foot and mouth disease, rinderpest, and bovine spongiform encephalopathy (BSE).

* At press time (June 29, 2004) the USDA reports BSE in the US as a case in an imported animal only. Please contact Invitrogen Technical Service or the USDA (www.usda.gov) for more information.

Meticulous collection and processing methods ensure high quality.

At Invitrogen, we maintain rigorous control of every step in the production of Gibco® FBS. This complete vertical integration, from collection to final product validation, ensures minimal risk of contamination with adventitious agents, lot-to-lot consistency, and superior performance.

We manufacture FBS in compliance with the Food and Drug Administration's (FDA) Quality System Regulation (cGMP) at our ISO-9001 certified facility in Grand Island, New York. In our U.S. and New Zealand facilities, we process raw FBS under the controls and conditions for the manufacture of medical devices as defined by the FDA. Comprehensive documentation ensures traceability and control of the process.

Using aseptic cardiac puncture procedures, we collect serum into bags specifically designed to improve clotting efficiency and serum yield.

We then quickly refrigerate the raw material, separating, evaluating and filtering it according to our exacting specifications. A typical batch is 1,000 L–1,600 L; some sources permit batch sizes up to 2,000 L. Following final filtration, which removes bacteria without removing critical serum components, we aseptically dispense the serum into sterile bottles.

We then label and freeze the final product, placing it in quarantine until all quality control tests have been completed.

Our Process Engineering department fully validates all procedures and processes to ensure quality and reproducibility. Our Quality Systems department can trace raw materials back to the original supplier and abattoir where they were collected.

Only FBS that meets all of our stringent manufacturing and finished product specifications is approved for sale.

List A Diseases**	AUS	C. AM	MEX	NZ	USA
African horse sickness	●	✔	●	●	●
African swine fever	●	✔	●	●	●
Bluetongue	●	✔	●	●	●
Classical swine fever	●	✔	●	●	●
Contagious bovine pleuropneumonia	●	✔	●	●	●
FMD (foot and mouth disease)	●	●	●	●	●
Highly pathogenic avian influenza	●	✔	●	●	
Lumpy skin disease	●	✔	●	●	●
Newcastle disease		✔	●	●	
Peste des petits ruminants	●	✔	●	●	●
Rift Valley fever	●	✔	●	●	●
Rinderpest	●	●	●	●	●
Sheep pox and goat pox	●	✔	●	●	●
Swine vesicular disease	●	✔	●	●	●
Vesicular stomatitis	●	✔	●	●	

● **Countries in which the disease has never been reported or diseases not report during 2003/2004.** *In 2002, World Animal Health reports on the animal health status, disease control methods and tables of incidence of List A diseases. Office International des Epizooties, 2004*

✔ **Refer to the World Animal Health Report 2002 for specific disease status for Central America.**

** List A diseases are transmissible diseases which have the potential for very serious and rapid spread, irrespective of national borders; which are of serious socio-economic or public health consequence; and which are of major importance in the international trade of animals and animal products. For more information visit the web site of the Office International des Epizooties: www.oie.int.

Special programs and services reduce serum variations.

While we dramatically reduce lot-to-lot variations of our Gibco® FBS through our carefully controlled and validated methods of serum performance and quality testing, we recognize that some cell types are sensitive to slight variations in serum. Therefore, we offer several additional ways to minimize the effect of these minor variations on your research:

Serum Matching Program

You'll never again have to perform time-consuming tests on over-the-counter purchases of reserved lots of serum. Simply tell us the specifications and performance characteristics you require, and we will deliver serum that matches your needs based on your applications, specifications and performance characteristics including:

Cloning Efficiency

We test FBS for ability to support cloning and growth of murine myeloma cells and derived hybridomas.

This is appropriate for most applications where low-density cloning of non-adherent cells or hybridoma development and monoclonal antibody (MAb) production are of primary interest.

Plating Efficiency

We employ transformed human cell lines to determine the suitability of FBS for attachment and proliferation of adherent cell lines compared to previously qualified FBS.

This is suggested for applications using continuous transformed cells at low or normal densities, and when performing clonal selections.

Growth Promotion

We test FBS for its ability to support the proliferation of fastidious human diploid fibroblasts through multiple subcultures.

This is useful in determining the lots that are most conducive to supporting growth and viability of difficult-to-grow, adherent, normal, primary, or established cell lines.

Reserve Serum Testing

Our reserve serum testing program allows you to obtain a sample of FBS to test in your own application. While you are testing the sample, we will hold your specified quantity until your assessment is complete. The minimum volume we will set up on reserve is:

- 40 x 100 ml
- 10 x 500 ml
- 15 x 1,000 ml

We usually hold serum for four weeks. If you require a longer test period, please let us know at the time you make your reserve request.

Gamma-Irradiated Sera

At your request, we will gamma-irradiate serum to inactivate any residual common bovine viruses and mycoplasmas that may be present. We have validated a process for utilizing gamma irradiation to inactivate viruses and mycoplasmas in animal serum, including FBS, newborn calf, porcine and equine sera (3).

We have demonstrated that physiochemical properties and cell culture performance of serum is not altered by gamma irradiation at levels established by European and FDA guidelines for virus titer reductions (4,5).

References

1. Barile, M.F. and Kern, J. (1971) *Proc. Soc. Exp. Biol. Med.* 138, 432.
2. Chen, J.R. (1977) *Exp. Cell. Res.* 104, 255.
3. Daley, J.P., *et al.* (1998), *Focus*, 20.3, 86 "Virus Inactivation by Gamma Irradiation of Fetal Bovine Serum."
4. ICH Topic Q5A, "Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human and Animal Origin," 1997.
5. "Design, Contribution and Interpretation of Studies Validating the Inactivation and Removal of Viruses," CPMP/BWP/268/95, February, 1996.

Quality Control Tests

We perform these quality control tests on each production lot, depending on the use of the serum.

Performance

	Certified FBS	Heat-Inactivated Certified FBS	Qualified FBS	Heat-Inactivated Qualified FBS	Dialyzed FBS	Ultra-Low IgG FBS**	ES Cell-Qualified FBS**
Relative Cloning Efficiency Assay Confirms ability of FBS to supportcloning and growth of murine myeloma cells and derived hybridomas.	●	●	●	●	●	●	●
Relative Plating Efficiency Assay Confirms ability of FBS to grow continuous adherent cell lines using human transformed cells.	●	●	●	●	●	●	●
Relative Growth Promotion Assay Confirms ability of FBS to supportthe proliferation of fastidious human diploid fibroblasts throughmultiple subcultures.	●	●	●	●	—	●	●
Sf9 Cell Growth Promotion Assay Ensures ability to grow Sf9 cells.	●	●	▲	▲	—	—	—

Embryonic Stem Cell Performance Assays

	Certified FBS	Heat-Inactivated Certified FBS	Qualified FBS	Heat-Inactivated Qualified FBS	Dialyzed FBS	Ultra-Low IgG FBS**	ES Cell-Qualified FBS**
Relative Plating Efficiency Assay Measures ability to initiate and support Embryonic Stem (ES) cell colonies when the ES cells are plated at a very low density in growth medium containing 10% FBS with no additional growth factors.	—	—	—	—	—	—	●
Cytotoxicity Assay Measures ability of ES and feeder cells to grow when plated at a very low density in growth medium containing 30% serum.	—	—	—	—	—	—	●
Relative Morphology and Differentiation Assay Measures ability to support the growth of undifferentiated ES cell colonies.	—	—	—	—	—	—	●

Key

Symbol	Description
●	Indicates test performed and passed.
—	Indicates test not performed.
▲	Indicates test performed and passed on selected U.S. sourced and USDA approved products.
C & R	Indicates check and record.
*	Indicates test performed and passed on Australian sourced products only.
**	These products are for research use, and where appropriate, as raw material components in further cell culture manufacturing applications. They are not intended for human or animal diagnostic, therapeutic, or other clinical uses, unless otherwise stated.

Chemical and Physical

	Certified FBS	Heat-Inactivated Certified FBS	Qualified FBS	Heat-Inactivated Qualified FBS	Dialyzed FBS	Ultra-Low IgG FBS**	ES Cell-Qualified FBS**
Biochemical Profile 22 key biochemical levels are determined through chemical analysis.	●	●	*	*	—	—	—
Bovine IgG (µg/ml)	—	—	—	—	—	< 5	—
Electrophoretic Profile Tested for normal characteristic, which confirms serum identity and integrity.	●	●	●	●	●	●	●
Endotoxin (EU/ml) Determined for each lot using an automated limulus amoebocytelysate (LAL) method.	≤ 10	≤ 10	≤ 50	≤ 50	≤ 50	≤ 50	≤ 50
Glucose (mg/dl)	—	—	—	—	≤ 5	—	—
Hemoglobin (mg/dl) Measured spectrophotometrically.	≤ 15.0	≤ 15.0	≤ 25.0 ≤ 30.0 (Aus)	≤ 25.0 ≤ 30.0 (Aus)	≤ 25.0	≤ 25.0	≤ 25.0
Determination of % Oxyhemoglobin	≥ 70%	≥ 70%	C & R *	C & R *	—	—	—
Hormone Profile Five hormone levels are determined.	●	●	*	*	—	—	—
Osmolality (mOsm) Tested using freezing point depression.	280-340	280-340	280-340	280-340	260-310	C & R	280-340
pH	6.9-7.8	6.9-7.8	6.9-7.8	6.9-7.8	6.9-7.8	6.9-7.8	6.9-7.8
Total Protein (gm/dl) Used to confirm animal age.	3.0-5.0	3.0-5.0	3.0-5.0	3.0-5.0	3.0-5.0	C & R	3.0-5.0

Adventitious Agents

	Certified FBS	Heat-Inactivated Certified FBS	Qualified FBS	Heat-Inactivated Qualified FBS	Dialyzed FBS	Ultra-Low IgG FBS**	ES Cell-Qualified FBS**
Bacteria and Fungi Confirms absence of noted contamination as noted in the current edition of the *United States Pharmacopeia*.	●	●	●	●	●	●	●
Bacteriophage Aquantitative bacteriophage plaque assay is performed using an appropriate *E. coli* strain.	●	●	*	*	—	—	—
Mycoplasma Tested by the method of Barile and Kern (1) (a large volume, direct inoculation method), and the Hoechst fluorescent DNA Stain (2).	●	●	●	●	●	●	●
Virus Testing is performed in full compliance with the Code of Federal Regulations (9 CFR, Section 113.53([113.46, 113.47]).	●	●	●	●	●	●	●
Bovine Viral Diarrhea (BVD) Neutralization Assay	—	—	—	—	—	●	—

Sera Descriptions, Applications and Sources

Product	Description/Usage Guidelines	Source	Cat. No.	Size
Certified FBS	• Undergoes special biochemical/hormonal profile and bacteria tests. Guaranteed low endotoxin (≤ 10 EU/ml) and low hemoglobin (≤ 15 mg/dl). • Use with your most sensitive, precious cells.	United States	16000-036 16000-044 16000-069	100 ml 500 ml 1,000 ml†
Certified, Heat-Inactivated FBS	• Heated for 30 minutes at 56°C with mixing to inactivate the complement. • Especially suited to immunological work.	United States	10082-139 10082-147 10082-170	100 ml 500 ml 1,000 ml†
Qualified FBS	• Our most popular FBS product. High quality and exceptional value. • Suitable for general applications, especially those that do not require defined biochemical/hormonal profiles or bacteriophage testing. • Endotoxin ≤ 50 EU/ml • Hemoglobin ≤ 25 mg/dl	United States	26140-087 26140-079 26140-095	100 ml 500 ml 1,000 ml†
		Australia	10099-133 10099-141 10099-158	100 ml 500 ml 1,000 ml†
		Countries that meet USDA importation requirements (Mexico, Central America)	10437-010 10437-028 10437-036	100 ml 500 ml 1,000 ml†

Product	Description/Usage Guidelines	Source	Cat. No.	Size
Qualified, Heat-Inactivated FBS	• Heated for 30 minutes at 56°C with mixing to inactivate the complement. • Especially suited to immunological work.	United States	16140-063 16140-171 16140-089	100 ml 500 ml 1,000 ml†
		Australia	10100-139 10100-147 10100-154	100 ml 500 ml 1,000 ml†
		Countries that meet USDA importation requirements (Mexico, Central America)	10438-018 10438-026 10438-034	100 ml 500 ml 1,000 ml†
Dialyzed FBS	• Dialyzed by Tangential Flow filtration utilizing a 10,000 MW cutoff. • Performance tested for cloning and plating efficiency.	United States	26400-036 26400-044	100 ml 500 ml
Ultra-low IgG FBS**	• Ideal for radiolabeling assays. • IgG levels are less than 5 µg/ml, and the BVD antibody titer is low or not detectable.	United States	16250-086 16250-078	100 ml 500 ml
ES Cell-Qualified FBS**	• Suitable for antibody production and veterinary applications. • Specially tested for the ability to sustain undifferentiated cellular morphology of embryonic stem cells. • Crucial for the successful maintenance of embryonic stem cells.	United States	16141-061 16141-079	100 ml 500 ml
		Countries that meet USDA importation requirements (Mexico, Central America)	10439-016 10439-024	100 ml 500 ml

All of the products listed here are packaged in E-Z Hold™ plastic bottles.

† *Available upon request.*

Reliability is everything.

Reliable quality. Reliable supply. Reliable consistency. Reliable support.

When you select a provider of Fetal Bovine Serum, reliability is undoubtedly your foremost consideration.

You and researchers everywhere agree. That's why Gibco® Fetal Bovine Serum is the FBS of choice—worldwide.

You know that Gibco® FBS provides excellent cell culture performance demonstrated by consistent, reproducible cell growth.

You trust Gibco® FBS to be of the highest quality. To be readily available. To be consistent lot-to-lot. To be supported by technical and regulatory expertise.

You have always relied on Gibco® FBS. And you can continue to do so with complete confidence.


GIBCO
Invitrogen Corporation

CERTIFICATE OF ANALYSIS

Catalogue Number: 16000-044
Lot Number: 1108713
Storage Temperature: -5 to -20C
Expiration Date: 30 July 08

Fetal Bovine Serum, Certified
Origin: United States
Performance, Mycoplasma, Virus, Bacteriophage and Endotoxin tested

triple 0.1 micron filtered

NOTICE: Effective 9/14/98, the pH specification for this product has been changed from 6.9 - 7.4 to 6.9 - 7.8. Should you have any questions, please contact Technical Services at 1-800-828-6686.

For in vitro diagnostic use. CAUTION: Not for human or animal therapeutic use. Uses other than the labeled intended use may be a violation of Federal law.

We certify that all Fetal Bovine Sera meets USDA requirements for abattoir-sourced animals, traceability and country of origin. ABBATOIR-SOURCED ANIMALS: All fetal blood is collected from fetuses derived from healthy dams that have passed pre and post mortem certified veterinary inspection. TRACEABILITY: All Fetal Bovine Sera is traceable by date and location of collection. COUNTRY OF ORIGIN: Fetal Bovine Serum collected in the United States is from USDA approved and inspected slaughter establishments. The United States is recognized by the USDA as being free of foot and mouth disease, rinderpest and bovine spongiform encephalopathy.

GIBCO cell culture liquid products are prepared by an aseptic process for which each step has been validated to ensure that all products meet the industry standard sterility assurance level of 10^-3; i.e. product that demonstrates a contamination level of no more than 1 of 1,000 units during the manufacturing process. The highest level of sterility assurance (equal to or greater than 10^-6) cannot be achieved without terminal sterilization which is harmful to the performance of cell culture products.

NOTICE: Since our sera are not pre-aged before filtration, turbidity or flocculent debris may develop upon thawing or storage. This condition does not adversely affect performance characteristic of the serum.

Testing is listed in alphabetical order.

TEST	SPECIFICATION	RESULT	UNITS
* Alkaline Phosphatase	Check and Record	279	u/L
* Bacteriophage Testing	Check and Record	Negative	
* Bicarbonate	Check and Record	20.0	MMOL/L
* Bilirubin (Total)	Check and Record	0.40	mg/dL
* Blood Urea Nitrogen (BUN)	Check and Record	13	mg/dL
BUN/Creatinine Ratio	Check and Record	4.1	
* Calcium	Check and Record	13.40	mg/dL
* Chloride	Check and Record	101	MMOL/L
* Cholesterol	Check and Record	<45	mg/dL
* Creatinine	Check and Record	3.20	mg/dL

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GIBCO
Fetal Bovine Serum
Certified
Origin: United States
Invitrogen Corporation

Each imported shipment of Gibco® FBS is accompanied by a Certificate of Analysis detailing USDA requirements, origin, storage temperature, expiration date and lot specific testing specifications.