Frequently Asked Questions (FAQs): FBS

What exactly is serum?

Serum is the liquid fraction of clotted whole blood. Unlike plasma, no anti-coagulant will have been added to the blood following collection from the animal. Serum is centrifuged to separate the clot from the liquid phase, resulting in a product that is depleted of cells, fibrin, and clotting factors.

What is the age range criteria for animal serum?

Bovine serum is categorised based on the age of the animals when a serum collection is made. The age of the animal is an important consideration because it impacts on the characteristics of the serum:

- Foetal bovine serum comes from foetuses
- Newborn calf serum comes from calves less than three weeks old
- Calf serum comes from calves aged between about three weeks and one year old
- Adult bovine serum comes from older cattle (i.e., older than 12 months)
- Donor bovine serum comes from donor animals which can be up to three years old

FBS is the most sought after and most costly serum. It has the advantage over other sources of having the lowest antibody levels and high growth factor concentrations.

What are the alternatives to using FBS?

Additional sources of serum are available and are generally more cost-effective options. These could also be described as FBS alternatives and can be used where budget restrictions dictate the use of cheaper material, or where applications permit the use of serum where levels of antibody and endotoxin will be higher. Alternatives include:

- Newborn calf serum - Useful for the culture of most mammalian cell lines
- Calf serum - Useful for fermentation process, as a stabiliser and control
- Adult bovine serum - Traditionally this is used as an additive to cell culture media and as a control
- Donor bovine serum - Used for the same purposes as Calf serum but will show lower levels of endotoxin. These donor herds are also carefully monitored as to diet to ensure that the resulting serum product is of the highest quality.
- Serum-free media formulations

Who is the ISIA and why is it important?

The ISIA (International Serum Industry Association, www.serumindustry.org) has established industry standards and a certification program with the aim of helping sera users substantiate the integrity of supply of FBS and other animal sera. Major companies that collect and sell FBS globally (including LSP) are members of the ISIA.

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The ISIA's mission is to 'establish, promote and assure compliance with uncompromised standards of excellence and ethics in the business practices of the global animal serum and animal derived products supply industry.' Their primary focus is on 'safety and safe use of serum and animal derived products through proper origin traceability, truth in labelling and appropriate standardization and oversight.'

As a user of sera, you can be sure that the FBS you receive from LSP is from the origin specified on the product label. Unless otherwise stated in the COA and product label, the FBS has also not been mixed with any other material.

What does it mean to be ISIA Traceability Certified?

Certification demonstrates full compliance with ISIA traceability standards, following an independent audit. As an ISIA Traceability Certified company, LSP processes establish traceability through the entire supply chain, from raw material collection to processing, filtration and order fulfilment. According to the ISIA traceability program, Certificates of Origin or Analysis must reflect all origins present (if in fact a mixture of sources exists) and also reflect the percentages of each.

What does it mean when FBS is labelled as USDA Grade or European (EU) Grade?

USDA Grade FBS is FBS of non-U.S.A. origin that the United States Department of Agriculture (USDA) considers to be acceptable for importation in the U.S.A. These countries are defined as being free of bovine spongiform encephalopathy (BSE) and foot and mouth disease (FMD). Countries include New Zealand, Australia, Mexico, and other Central American countries. With the exception of New Zealand (which can be imported without additional testing), serum must first be quarantined on importation prior to samples being tested at USDA facilities to ensure freedom from Bluetongue virus and, in the case of Australian serum, Akabane virus. The name 'USDA-approved' is misleading since the USDA does not 'approve' serum. What this actually means is that the serum has been safety tested in accordance with USDA methodology. The ISIA (International Serum Industry Association) is encouraging members to change labelling to reflect the actual country of origin without mention of 'USDA'.

EU Grade FBS is FBS of South American origin that is permitted for importation into the EU under Commission Regulation (EU) No 142/2011. This material is also permitted to be imported into certain countries in Asia. EU Grade is currently not permitted to be imported into the U.S.A. The ISIA is encouraging members to change labelling to reflect the actual country of origin of the serum.

What does the 'Country of Origin' refer to?

The country of origin for FBS refers to country in which the raw blood was collected.

Major FBS producing countries are Australia, Canada, Central America, New Zealand, South America and the U.S.A. While some countries may be considered more desirable sources of FBS than others, it is not true that FBS is of better quality from any given country. Desirability is linked to the disease status for each country (as described by the World Organization for Animal Health (OIE)) relevant to the application to which the serum

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is to be used. In addition, supply and demand plays a role making some sources of FBS more expensive than others. This is especially the case for New Zealand and Australia whose island nations have left the countries largely untouched by bovine diseases.

The OIE monitors the global incidence of animal disease including BSE and publishes this information on a regular basis. Regulatory authorities and processors use it as one of the critical determinants in deciding which countries may be used as a source of serum for certain applications with those sera acceptable for industrial use such as vaccine manufacture usually demanding the highest price in the market.

How can I be sure that the serum I'm using comes from the country I specify?

LSP states the origin of each batch of FBS on the product label. Furthermore, this same batch information is also provided on the Certificate of Analysis (COA). As an ISIA Traceability certified company, LSP can trace raw materials back to the original supplier and abattoir or donor farm where the material was collected. This provides absolute assurance the material is sourced from the country specified.

How is the serum industry regulated?

Wide-ranging regulations control all aspects of the production of serum and other animal derived products and their subsequent use. The European Union and the United States are major users of these materials with Japan, India and China emerging as major players. The main cattle producing countries are the United States and Canada, Australia and New Zealand and several South American nations. Animal health and welfare, slaughter conditions, hygiene and all subsequent treatments and processes are highly regulated and supervised by national veterinary authorities according to both national laws and the laws of the importing nations.

The animal by-products framework is defined by Regulation (EC) No 1069/2009 and the implementing Regulation (EU) No 142/2011. These regulations are intended to simplify requirements and reduce the administrative burden on Industry, with a particular focus on achieving a more risk-based approach in handling of those animal by-products destined for the manufacture of technical products and which are not intended to enter the food or feed chain. Regulation (EU) No 294/2013 has recently been added.

These regulations cover the importation, certification, handling and transportation requirements for 'raw' animal by-products, derived products, blood derived products and Intermediate Products and define when devices or products have reached their end point and/or are otherwise outside the scope of Regulation (EC) No 1069/2009.

The ISIA (International Serum Industry Association) has played an active role in discussion with various regulatory bodies in the evolution of these and other regulations.

What tests are carried out on FBS products?

Each batch of LSP FBS is tested to ensure freedom from bacteria, fungi, yeast, mycoplasma (*M. bovis, M. arginini and A. laidlawii*) and specific bovine viruses. Batches are also tested for the ability to support growth

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of specific cell lines. In addition, each batch is also tested for standard parameters. These include endotoxin, pH, osmolality, protein content, albumin, IgG and haemoglobin levels. Details for each batch are supplied on the Certificate of Analysis (COA).

Is FBS Tetracycline-free?

Some batches of serum from different countries will contain levels of tetracyclines in the serum. This is due to the fact that the animals have been fed tetracyclines in their diet prior to slaughter. This typically occurs where cattle are kept on feed lots, in countries such as the USA and Australia. In Brazil, cattle are mainly grass fed and, as such, will not have tetracycline present in the serum. We do not routinely test our FBS from Brazil for tetracyclines but this test can be performed, if required.

Which viral infections are batches of FBS tested for?

All LSP FBS is tested for Bovine Viral Diarrhoea Virus (BVD-V), Bovine Parainfluenza-3 virus (PI3), Infectious Bovine Rhinotracheitis (IBR) and Bovine Viral Diarrhoea Virus antibodies (BVD-AB).

Is LSP FBS sterile?

Each batch of LSP FBS is tested for the absence of bacteria, fungi, yeast, mycoplasma. LSP FBS is also sterile filtered through three sequential 100 nm (0.1 µm) pore size-rated filters. Results of microbe testing of each batch of serum is supplied in the COA. However, please note that sterility is not guaranteed after opening. The use of aseptic techniques during handling is recommended.

What level of quality assurance can I expect from LSP for FBS products?

The quality of FBS is inherently linked to the collection and processing methods used and not the country of origin. A closed-system collection method (cardiac or venepuncture) and rapid processing are essential to produce a quality product. Low levels of endotoxin and haemoglobin are excellent indicators of the care with which collection and processing have been carried out. LSP FBS typically has endotoxin levels of below 10 EU/mL with some batches having endotoxin levels of below 1 EU/mL.

- Every batch of FBS is rigorously controlled throughout the process, from collection to treatment and finally packaging. This ensures complete traceability right back to the source. LSG is an ISIA Traceability certified company.
- All our serum is collected and treated in accordance with current European regulations.
- Each batch is triple filtered to 0.1 micron prior to Quality Assurance Testing to ensure that the product is negative for bacteria, yeast, fungi, and mycoplasma. In addition, biological performance of final batches of sera is assessed for cell growth, plating efficiency, and cloning efficiency.
- Full batch documentation is available, including Certificates of Analysis and Certificates of Origin.

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Can my FBS be treated before shipping?

Yes. FBS is available as heat inactivated, gamma irradiated, dialysed and charcoal stripped material.

What does heat inactivation do to the serum?

FBS may be heat inactivated by heating to 56°C for 30 minutes to inactivate various components in the serum such as complement factors.

Should I heat-inactivate my serum?

At one time, heat inactivation was considered necessary because of concerns over the presence of contaminants in serum. However, the process of heat inactivation is known to degrade valuable biomolecules, such as growth factors, vitamins, and amino acids. Many protocols still call for serum to be subjected to heat treatment prior to use without consideration as to whether it remains desirable. Should it be required, LSP can provide heat inactivation as a custom processing option.

What pack sizes are available for FBS?

FBS is supplied in 500 mL bottles. Other pack sizes or presentations are also available on request e.g. 100 mL and 1 L bottles, or individual supplier packs.

Can I sample batches of FBS?

Yes. LSP offer samples of FBS for testing prior to selection of a suitable batch. Typical sample size is 50 mL and reservations are held for a period of four weeks, pending evaluation.

What is the shelf life for FBS?

FBS has a shelf life of 5 years from the date of manufacture, provided it is stored appropriately. We would recommend enquiring about the shelf life of each available batch if it is important to have a long shelf-life following purchase.

While there may be a drop off in growth promotion properties over time, the level of any change will depend on the cell type and assay conditions. Therefore, should a batch of serum be coming up to its original expiry date and it is still performing adequately, rather than destroy the material, LSP is happy to extend the expiry date by 12 months. This re-test may be performed on a rolling 12-month basis. This means that the considerable time and investment in batch testing of a large batch of material need not be wasted should the supply last longer than forecasted.

What is the recommended storage and handling for FBS?

Recommended storage is -20°C or below.

Protect serum from exposure to light.

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It is recommended to avoid freeze-thaw cycles as this can lead to a deterioration in serum qualities. Ideally, material should be thawed under controlled conditions and re-aliquoted into smaller volumes before re-freezing. It is not recommended to store or refreeze partially used serum as degradation is rapid if microbial contamination occurs. All biological material should be handled as potentially infectious. It is essential that universal precautions should be employed when handling FBS.

How is FBS shipped?

FBS will be shipped frozen, by overnight courier in polystyrene moulded boxes with dry ice unless we are specifically requested not to do so. This will ensure that the material arrives frozen in good condition.

What should I do if I get precipitation in my serum?

When serum is thawed, some precipitation may be seen. This is a normal phenome-non and it does not compromise the quality of serum in any way. To remove the precipitate, transfer the serum to sterile tubes and centrifuge for 5 mins at 400g.

To limit the amount of precipitation, we recommend that the serum is thawed in a refrigerator at 2-8°C. The serum should be regularly mixed during this process.

In the unusual event of serum arriving partially thawed, please note that it is inadvisable to refreeze from this state as partially thawed serum must be allowed to thaw completely at 4°C.

When the serum has thawed completely, gently invert the container several times to achieve thorough mixing and refreeze as soon as possible to -20°C. To avoid repeated freeze/thaw cycles dispense the serum into single use aliquots before freezing.

Support

Life Science Production is a division of Life Science Group Ltd.
Life Science Production is ISIA Traceability Certified.
Life Science Group Ltd is an ISO 9001:2015 and ISO 13485:2016 Certified Company

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