

Sera for Cell Culture

HIGHEST QUALITY, CONSISTENCY, TOTAL TRUST





Our ultra-modern production facilities guarantee the high quality of our serum products and help ensure the success of your research.

For almost 20 years PAA has been a manufacturer and supplier of high quality products for cell culture including, media, buffer solutions, reagents and, in particular, sera. Our serum products have previously been produced only in our state-of-the-art production facility in Pasching, Austria. In 2005 PAA acquired the production operations of Cansera (Canada) and Serum Ventures (Australia) and now have full serum collection and production in all three facilities providing PAA, and its customers, with true global manufacturing capabilities. As a result of the above, PAA has now secured its position as a world class supplier of animal and other sera for our research based and industrial customers in the rapidly expanding areas of biopharmaceuticals and vaccines.

All PAA's production facilities operate under strict cGMP guidelines and are registered with the FDA¹ (USA) and EDQM² (Europe). The PAA facility in Pasching has also been granted a pharmaceutical production licence by the Austrian MOH which will allow production of products for use in leading technologies such as stem cells and transplantation.

From collection of raw sera through to the final, sterile filtered, product PAA controls and documents all process's ensuring full traceability from the animal through to 'the bottle'. Full batch records including Certificates of Suitability, Certificates of Analysis and other batch release documents are available for all of our customers.

Total production transparency and Total product trust... the benchmarks of PAA Laboratories.

¹US Food and Drug Administration

²European Directorate for the Quality of Medicines



Serum

Still the 'Elixir' of Cell Culture Life

Since early 20th century scientists have been searching for methods to allow the isolation and growth of tissues and cells outside of the body in what we now term as *in vitro* conditions. In the late 1940's the first cell line (HeLa) was cultivated *in vitro* in a fluid mixture of chicken plasma, bovine embryo extract and serum from umbilical chord blood. This crude mixture was the forerunner of today's modern cell culture media.

The ideal culture medium simulates the exact *in vivo* conditions. In practice this can only be achieved to a limited extent as the physiological conditions required to cultivate tissues, cells and living organisms are extremely complex.

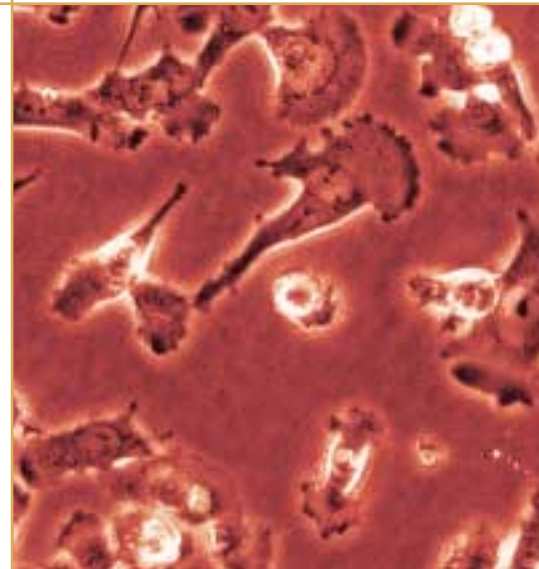
Serum provides all of the growth factors, vitamins, co-factors, hormones, attachment factors (fibronectin, laminin), transport factors (albumin, globulin, transferrin), nutrients (nucleosides, amino acids, fatty acids, lipids), trace elements and other factors which limit free radicals, toxins and heavy metals. Serum is a very complex product and only a small percentage of the components have been fully identified. Therefore it remains the most effective growth product for cell culture available today.

Most sera used in cell culture are from some form of animal, mainly bovine origin. This brings some disadvantages such as antibodies which may impair or damage cell growth, the possibility of presence of adventitious animal viruses and the possible contamination with endotoxins and mycoplasmas which can damage fragile cell lines.

However modern techniques used both in the collection of the raw blood through to vastly improved production and filtration techniques have resulted in much higher quality sera free from endotoxins, mycoplasmas etc. being now offered to cell culture scientists.

From raw material collection through to final finished product PAA production facilities ensure that only sera with the highest quality and levels of safety are manufactured.

The 1980's and 1990's saw the development of serum free media, however there are still only a very few cell specific serum free media available and the use of sera still remains an essential part of both research and biopharmaceutical/vaccine production.



The addition of serum to culture medium ensures a natural cell cycle and metabolism.

Animal Sera | Origin

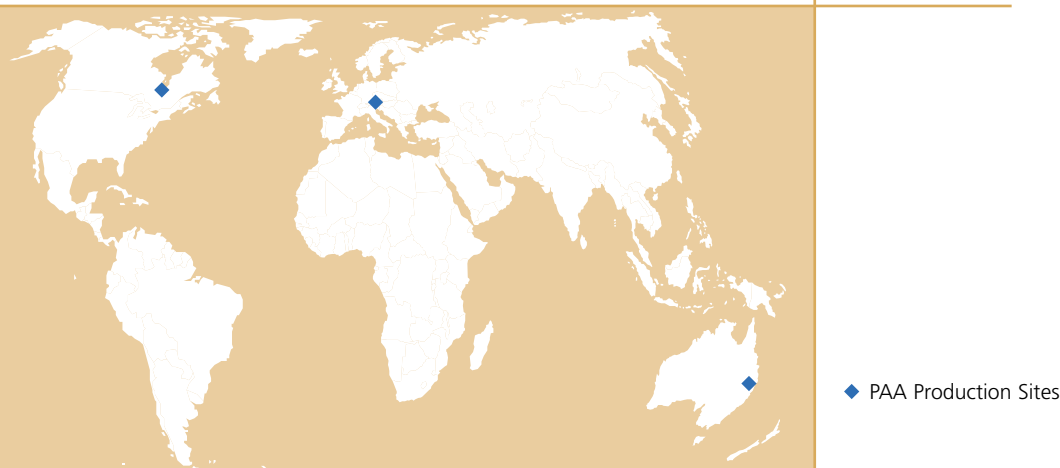
Since the first occurrence of Bovine Spongiform Encephalopathy (BSE or Mad Cow Disease) in the UK in the mid 1980's, the safety requirements for the use of animal sera have become far more stringent. However it must be stressed that bovine sera, and in particular, Foetal Bovine Serum, are classed as 'low risk products' as far as Transmissible Spongiform Encephalopathies (TSE) are concerned. It has been shown that the causative agent of BSE, a prion, cannot pass the placental barrier of the pregnant cow and as such there is no risk involved with Foetal Bovine Serum. There is a slightly higher risk with sera collected from older animals in such products as Newborn Calf, Calf Serum and Adult Bovine Serum although it is true to say that even this risk level is less than minimal. The causative agent of BSE is closely linked to brain and spinal chord tissues of cows and have not been detected in the blood of these animals.

BSE is only one of a number of animal viruses which may be present in animal sera. Diseases such as Foot and Mouth (FMD), Rabies, Herpes and others can all affect cattle worldwide. PAA only selects raw serum from sources where the risk of these diseases is absolutely minimal. We offer FBS and other animal sera under the following classifications:

EU approved: Cost effective sera manufactured from raw materials sourced mainly from Latin American countries such as Brazil and Argentina.

USDA approved: Sera manufactured from raw materials sourced from Central American countries such as Mexico and Panama.

PAA also produces sera originating exclusively from the **USA, Canada and Australia**.



The European Union (EU) will only permit the import of bovine products, including blood and sera, from countries certified by the EU as 'specific disease free'. This criteria is met by materials from USA, Canada, Australia, New Zealand, certain countries in Central America (eg. Mexico & Panama) and Latin America (eg. Brazil & Argentina). The EU approved origins of animal sera, and products manufactured using EU approved origin sera including South American origins, can be freely moved between all EU member countries and many other countries outside of Europe where the USDA or FDA regulations are not required.

The main authority responsible for these products in the USA is the United States Department of Agriculture (USDA). Serum and finished products manufactured from sera of USA, Australian, New Zealand and USDA approved origins, if processed in the USA, Australia or New Zealand will be allowed to enter into the USA. This is also the case for researchers who are working on research projects with USA based researchers.

To meet your requirements PAA has manufacturing sites of FBS and other animal sera in Europe, Australia and North America.

Animal Sera | Collection

Most animal sera, including FBS, used in cell culture are a by-product of the meat processing industry. Blood is collected at the abattoir, centrifuged to separate the blood cells from the serum, frozen and then shipped to our production facilities for further processing.

In the case of Foetal Bovine Serum skilled operators remove the blood from the foetus by aseptic cardiac puncture. This process is carried out in special areas within the abattoir to reduce the possibility of bacterial contamination which can result in the presence of endotoxin in the serum. The raw FBS is then carefully centrifuged to separate the blood cells from the serum. It is at this stage that PAA use process's which ensure that sera with only low levels of haemoglobin are processed. After centrifugation the raw serum is frozen and then shipped to our processing facilities. Before freezing, samples are removed and tested for endotoxin and haemoglobin levels.

Donor sera are collected by venepuncture from carefully controlled herds of live animals. All animals in these donor herds are regularly checked by registered veterinarians for signs of diseases. Any animal showing signs of sickness is immediately isolated and placed into quarantine. All animals in donor herds have very high levels of animal husbandry care and controlled feeding diets to ensure high quality sera is obtained. Diet can be a contributing factor as to whether the serum is high in growth promoting properties.

All raw sera are then processed in PAA's state-of-the-art, cGMP compliant, FDA registered production facilities. The raw serum is thawed and transferred to our 2.600 litre pooling tank and then mixed to create a true pool. The serum is passed through a cascade of triple 0.1 micron filters before moving into our class 100, fully automated, bottling facilities. After bottling it is then labelled with full product code, batch number and other details including a bar code. The finished labelled, sterile filtered product is taken to our rapid cooling freezer and frozen at -20 °C. The storage is obtained in our carefully controlled freezer store rooms.

All production process's used by PAA have been validated and at each stage through the production cycle batch documentation is provided.

Each batch of sera is extensively tested by our QC department. Full details of specifications and test results are available on the corresponding Certificate of Analysis (CoA).

Foetal Bovine Sera which must comply with higher safety standards undergo additional animal virus testing in line with 9CFR and EP³ regulations. The "Pharma Grade" FBS from PAA meets these stringent regulations with sera of both USA and Australian origin being available. This grade of FBS is particularly suitable for use in industrial production but can also be used in research in areas such as advanced cell therapy.

All FBS products are packaged in gamma irradiated 100 & 500 ml PET bottles. Packaging in alternative containers and volumes is also available upon request.

PAA offers many other treatments for FBS and other sera and these are shown in the following pages.



Each individual batch of serum is subjected to an exhaustive programme of testing.

³European Pharmacopoeia

Animal Sera | Further Processing

Numerous innovative techniques and methods are used in modern biopharmaceutical research. Many of these place specific demands on the sera used in the cell culture. Some of our serum is thus post-treated in order to make it particularly suitable for specific applications. Some of these treatments eliminate viruses and other microorganisms, so increasing the biological safety of the sera. Other treatments remove various natural serum constituents which disrupt certain analytical techniques or assays. We furthermore carry out testing to identify batches of serum having characteristics which make them ideal for specific applications or certain cell lines.



Using this patented apparatus developed by PAA, sera are subjected to UV light irradiation under controlled conditions.

HEAT INACTIVATION

Before the advent of FBS, cells were cultivated in more adult sera which contained components such as antibodies, complement factors and higher levels of animal viruses which could damage cell growth. To remove these components and viruses many laboratories used a Heat Inactivation (HI) process. The use of Foetal Bovine Serum together with vastly improved serum production process's has now, to a large extent, removed the need to HI serum. For other, more adult serum, then heat inactivation may still be required. If you require to heat inactivate your serum then a carefully controlled process must be followed in order to avoid damaging the cell growth promoting properties of the serum and reducing the formation of unwanted precipitates.

The process involves heating the serum in a shaking waterbath at exactly 56 °C for 30 minutes. The shaking will help avoid the formation of protein and other forms of precipitates. After 30 minutes the serum is then cooled back down to room temperature as quickly as possible to avoid excessive exposure to heat which can damage growth factors, vitamins etc. The heat inactivation process will inactivate the complement system, antibodies and other active enzymes such as lactate dehydrogenase (LDH). It is therefore recommended to use heat inactivated serum for immunoassays or if LDH is to be measured in the cell culture supernatant as an indicator of cell damage.

UV IRRADIATION

UV light of a wavelength of 254 nm damages nucleic acids, so killing mycoplasmas and viruses, but not impairing the biological activity of the serum. The gain in biological safety is greater than that obtained by gamma irradiation.

PAA is the only company to have developed a patented and certified process for UV irradiating serum. Serum treated in this way is known by the name "Mycoplex". Mycoplex serum is 100% mycoplasma free while fully retaining its growth promoting action. As a result, it is ideal for culturing particularly sensitive cell lines or for primary cell culturing.

DIALYSIS

This process brings about a distinct reduction in the serum's content of molecules with a molecular weight of < 10 kDa, for example nucleotides and amino acids. This involves dialysing the serum against physiological saline through a membrane with a cut-off of 10 kDa. Dialysed serum is suitable for use within incorporation studies, in which the addition of labelled nucleotides or amino acids is intended to reveal information about biochemical processes in the cell. The molecules contained in conventional serum would compete with the labelled molecules and so jeopardize the success of these studies. Various hormones are also removed from the serum by dialysis. This is an important factor in many receptor studies, as there is a risk that hormones from the serum will displace the test substances from the binding sites of the corresponding receptors.

GAMMA IRRADIATION

Sterile filtration can ensure that sera are largely free of microorganisms, however more stringent serum sterility requirements apply to applications such as virus or vaccine production. Such requirements are met by gamma irradiation with cobalt 60 (^{60}Co) which further reduces or eliminates the viruses and mycoplasmas which may be present in the serum after filtration.

Bottles of serum are generally irradiated on pallets. In order to achieve a dose of for example 35 kGy in the centre of such a pallet, it must be irradiated with a total dose of 50 kGy. The increased irradiation level generates extra heat which can result in damage to the serum, particularly in the outer boxes. This non-uniform irradiation of the bottles also impairs the homogeneity of the batches of serum.

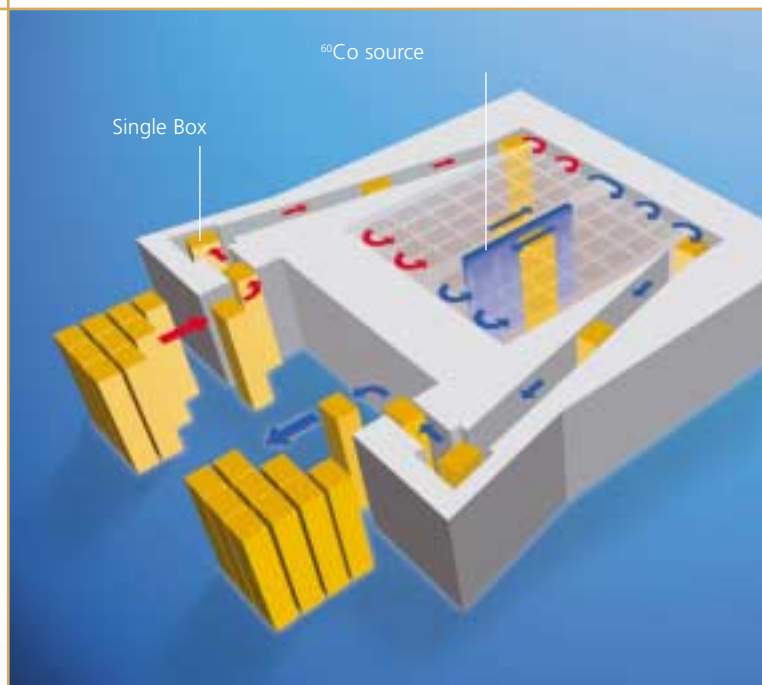
To avoid these problems PAA has introduced single box irradiation. In this process, small packaging units are continuously conveyed past the radiation source. Each individual bottle of serum is exposed to a dose of 35 kGy to at most 38.7 kGy. The sensitive growth factors are protected and the homogeneity of batches of serum is retained.

IgG REDUCTION

The production of monoclonal antibodies with hybridoma cells places particular demands on the culture medium, as conventional FBS may bring about a concentration of IgG antibodies in the medium which impairs the isolation and purification of monoclonal antibodies. PAA therefore supplies a specific FBS from which immunoglobulins G have been removed by hydrophobic charge induction chromatography (HCIC). This gentle process minimizes any reduction in the serum's growth promoting action, as it removes many fewer growth factors from the serum than the conventional method of affinity chromatography with protein A sepharose.

PRE-TESTING

Pre-testing identifies batches of serum which are particularly suitable for specific cell cultures because of their natural, individual characteristics. Sera with an extremely low endotoxin content is supplied under the name "PAA Clone". The low endotoxin content is particularly favourable for culturing primary or hybridoma cells. We can also supply sera which are largely free of tetracyclines or tetracycline derivatives and are so ideally suitable for use in Tet on/off expression systems. PAA provides sera which testing has revealed to be particularly suitable for culturing embryonal stem cells (ES cells) or amnion and chorionic villi cells in cytogenetics.



The irradiation source is located in the centre of the gamma irradiation facility. The products are continuously driven through the plant in small packaging units (single boxes).

Product	Cat. No.	Volume
Foetal Bovine Serum, Standard Quality		
Australian origin	A11-501	100 ml
	A15-501	500 ml
USA origin	A11-201	100 ml
	A15-201	500 ml
Canadian origin	A11-701	100 ml
	A15-701	500 ml
USDA approved	A11-301	100 ml
	A15-301	500 ml
EU approved*	A11-101	100 ml
	A15-101	500 ml



Product	Cat. No.	Volume
Foetal Bovine Serum GOLD		
Australian origin	A11-551	100 ml
	A15-551	500 ml
USA origin	A11-251	100 ml
	A15-251	500 ml
Canadian origin	A11-751	100 ml
	A15-751	500 ml
USDA approved	A11-351	100 ml
	A15-351	500 ml
EU approved*	A11-151	100 ml
	A15-151	500 ml

Foetal Bovine Serum, Standard Quality

This is conventional Foetal Bovine Serum (FBS; synonym: Foetal Calf Serum (FCS)). It acts not only as a growth promoting additive to your cell culture media, but also as a stabilizer in diagnostic assays, for surface coating culture vessels or for inactivating trypsin. It supports most cell lines and is tested for viruses and microorganisms. Like almost all our Foetal Bovine Sera, this serum is available in 5 categories of origin.

- Additive for cell culture media
- Stabilizer
- Surface coating
- Inactivation of trypsin

Foetal Bovine Serum GOLD

Foetal Bovine Serum GOLD is completely defined, but is not a synthetic product, and contains no additives from other sera. The serum is chromatographically purified and fractionated. The individual constituents are then recombined in a defined composition. Batch-to-batch variation is thus a thing of the past. Batch testing is not required for FBS GOLD and batch reservation is unnecessary.

FBS GOLD is ideally suited to all cell cultures, calibration and fermentation operations or diagnostic assays.

FBS GOLD is distinguished by a particularly low content of IgG antibodies.

FBS GOLD is one of PAA's most significant and innovative product developments in recent years.

- Completely defined
- No batch testing
- No batch-to-batch variation
- No batch reservation
- Multi-purpose

* Not available in North America due to USDA restrictions

PA has in its portfolio a wide range of special Foetal Bovine Sera. Due to special treatments, sera tailored to specific biotechnology applications can be supplied. We offer special processes which enhance the level of safety with regard to contamination with viruses or other microorganisms. Others serve to remove certain constituents from the sera which have a disruptive action in specific analytical methods. We can also identify batches of serum which are particularly suitable for specific applications because of their individual, natural characteristics.

Foetal Bovine Serum, Heat Inactivated

Heat inactivates the complement system and many enzymes in this serum (see page 6) which has thus proved particularly valuable in immunoassays or certain enzyme tests. It is, however, also suitable for all conventional applications, such as a culture medium additive, as a stabilizer or for coating culture vessels.

- Additive for cell culture media
- Stabilizer
- For immunoassays
- Ideal for enzyme tests

Product	Cat. No.	Volume
Foetal Bovine Serum, Heat Inactivated		
Australian origin	A11-504	100 ml
	A15-504	500 ml
USA origin	A11-204	100 ml
	A15-204	500 ml
Canadian origin	A11-704	100 ml
	A15-704	500 ml
USDA approved	A11-304	100 ml
	A15-304	500 ml
EU approved*	A11-104	100 ml
	A15-104	500 ml

Foetal Bovine Serum, Dialysed

Dialysis removes many hormones from this serum (see page 6). The content of nucleotides and amino acids is also distinctly reduced. These properties make dialysed serum ideally suitable for use in incorporation or receptor studies.

- Additive for cell culture media
- Ideal for incorporation studies
- Ideal for receptor studies

Product	Cat. No.	Volume
Foetal Bovine Serum, Dialysed		
Australian origin	A11-507	100 ml
	A15-507	500 ml
USA origin	A11-207	100 ml
	A15-207	500 ml
Canadian origin	A11-707	100 ml
	A15-707	500 ml
USDA approved	A11-307	100 ml
	A15-307	500 ml
EU approved*	A11-107	100 ml
	A15-107	500 ml

* Not available in North America due to USDA restrictions

Product	Cat. No.	Volume
Foetal Bovine Serum, IgG Stripped		
USA origin	A11-206	100 ml
	A15-206	500 ml
EU approved*	A11-106	100 ml
	A15-106	500 ml

Foetal Bovine Serum, IgG Stripped

HI chromatography reduces the IgG content of the serum to below 5 µg/ml (see page 7). The gentle process ensures unimpaired growth promotion. FBS with such a low IgG antibody concentration is outstandingly suitable for hybridoma cell culture and the production of monoclonal antibodies.

- Additive for cell culture media
- Ideal for hybridoma cells
- Ideal for the production of monoclonal antibodies

Product	Cat. No.	Volume
Foetal Bovine Serum, Gamma Irradiated		
Australian origin	A11-503	100 ml
	A15-503	500 ml
USA origin	A11-203	100 ml
	A15-203	500 ml
Canadian origin	A11-703	100 ml
	A15-703	500 ml
USDA approved	A11-303	100 ml
	A15-303	500 ml
EU approved*	A11-103	100 ml
	A15-103	500 ml

Foetal Bovine Serum, Gamma Irradiated

Gamma irradiation further reduces or eliminates viruses and mycoplasmas and so enhances the biological safety of the sera (see page 7). This is thus particularly suitable for the production of biopharmaceutical and diagnostic products, including virus and vaccine production.

- Additive for cell culture media
- Ideal for biopharmaceutical production processes
- Ideal for the production of diagnostic products
- Ideal for virus and vaccine production

Product	Cat. No.	Volume
Foetal Bovine Serum, Mycoplex		
Australian origin	A11-505	100 ml
	A15-505	500 ml
USA origin	A11-205	100 ml
	A15-205	500 ml
EU approved*	A11-105	100 ml
	A15-105	500 ml

* Not available in North America due to USDA restrictions

Foetal Bovine Serum, Mycoplex

Irradiation with UV light reliably eliminates any mycoplasmas and UV-sensitive viruses which are present. PAA has patented its own validated process for this purpose which does not impair the growth promoting action of the serum (see page 6). FBS Mycoplex is the ideal FBS for all applications in which it is essential to rule out any mycoplasma contamination and for particularly sensitive cell lines or primary cells.

- Additive for cell culture media
- Guaranteed mycoplasma free
- For primary cells

Minimize your risk with Mycoplex:

Mycoplasmas growing on the surface of an infected cell.

Photo: M. Rohde, GBF Braunschweig; C. Uphoff, DSMZ, Braunschweig



Pre-tested Foetal Bovine Sera

These sera are not post-treated but, because of their individual, natural properties, are instead particularly suitable as a medium additive for culturing specific cell types (see page 7).

Foetal Bovine Serum, Tetracycline negative

These sera contain a maximum tetracycline or tetracycline derivative concentration of 0.5 µg/ml. They are particularly suitable for expression studies in Tet-on/Tet-off systems, in which a promoter is switched on or off by tetracycline, so enabling control of the expression of a cloned gene. This serum is also distinguished by its low endotoxin and IgG content.

- Ideal for expression studies in Tet-on/Tet-off systems

Foetal Bovine Serum, Amnion cell tested

These batches of serum are selected by quantitative growth assays with amnion and chorionic villi cells.

- Ideal for amnion and chorionic villi cells
- Suitable for lymphocytes
- For use in pre- and postnatal diagnostics
- For karyotype analyses
- For Fluorescence *In Situ* Hybridisation (FISH analysis)

Foetal Bovine Serum, ES cell tested

The selection criterion for this serum is the morphology of the stem cell colonies and elevated expression of the stem cell marker phosphatase.

- Supports the growth of undifferentiated ES cells
- Low nonspecific stimulation
- Ideal for many primary cells

Foetal Bovine Serum, PAA Clone

A serum with particularly low endotoxin content of below 1 EU/ml and a particularly elevated plating efficiency. This serum is ideally suitable for myeloma, hybridoma, endothelial and neuronal cells.

- Ideal for myeloma cells
- Ideal for hybridoma cells
- Ideal for endothelial cells
- Ideal for neuronal cells

Product	Cat. No.	Volume
Foetal Bovine Serum, Tetracycline negative		
USA origin	A11-209	100 ml
	A15-209	500 ml
EU approved*	A11-109	100 ml
	A15-109	500 ml



Part of a karyogram prepared from human amnion cells

Product	Cat. No.	Volume
Foetal Bovine Serum, Amnion cells tested		
	A11-110	100 ml
	A15-110	500 ml

Product	Cat. No.	Volume
Foetal Bovine Serum, ES cell tested		
	A11-208	100 ml
	A15-208	500 ml

Product	Cat. No.	Volume
Foetal Bovine Serum, PAA Clone		
USA origin	A11-202	100 ml
	A15-202	500 ml
EU approved*	A11-102	100 ml
	A15-102	500 ml

* Not available in North America due to USDA restrictions

Product	Cat. No.	Volume
Foetal Bovine Serum, Pharma Grade		
Australian origin	A11-511	100 ml
	A15-511	500 ml
Australian origin, Gamma Irradiated	A11-512	100 ml
	A15-512	500 ml
USA origin	A11-211	100 ml
	A15-211	500 ml
USA origin, Gamma Irradiated	A11-212	100 ml
	A15-212	500 ml

Foetal Bovine Serum, Pharma Grade

PAA Pharma Grade is the most intensively tested FBS and offers the customer the highest levels of safety particularly with regard to possible virus contamination. FBS Pharma Grade originates exclusively from the USA or Australia, both of which have the lowest levels of bovine disease. The entire production process is governed by the latest regulations:

- FDA's Code of Federal Regulations (9CFR)
- EMEA Guideline 1793/02, 743/00
- EP Monograph of Bovine Serum 5.4

When one of these guidelines is updated, PAA immediately adjusts its production process accordingly. The regulations require complete traceability of the final product right back to the abattoir and demand extensive testing with regard to sterility before and after filtration. Specifically, FBS Pharma Grade undergoes the following tests:

- Bluetongue Virus (BTV)
- Bovine Adenovirus (BAV)
- Bovine Parvovirus (BPV)
- Bovine Respiratory Syncytial Virus (BRS-V)
- Reovirus (Reo-3)
- Bovine Virus Diarrhoea Virus (z. B. BVD-V)
- Rabies Virus
- Parainfluenza Virus (PI-3)
- Bovine Herpes Virus (BHV-1 / IBR)
- BVD-1-AB und BVD-2-AB
- Rabies-AB
- Comparative BVD virus growth inhibition
- BVD-AB Interferences

Such an intensively tested serum is particularly suitable for applications with extremely high safety requirements. These include virus and vaccine production, the production of monoclonal antibodies, recombinant growth factors or reimplantation experiments. FBS Pharma Grade is used industrially for the production of biopharmaceutical products.

- Virus and vaccine production
- Production of monoclonal antibodies
- Production of recombinant growth factors
- Reimplantation experiments
- Advanced therapy



Bovine Sera

The Alternative to FBS

For many cell cultures, Foetal Bovine Sera is an ideal additive to the medium as it contains particularly high levels of growth factors. Their disadvantage is their comparatively high price. Robust cell lines may also be cultured with other, lower cost bovine sera. As a rule of thumb, the older the animals from which the serum was obtained, the lower the growth promoting action and the greater is the content of antibodies and protein. More moderate growth promotion than that provided by FBS may also be advantageous if there is a risk that, in the event of great multiplication, the cells will have to be passaged too frequently.



Neo-natal Foetal Bovine Serum

This serum is obtained from calves which are less than 12 hours old and have not yet been suckled with colostrum, as a result of which it contains very few antibodies. Neo-natal serum is the most similar to FBS and has an almost identically strong growth promoting action. It is also suitable for sensitive cell cultures.

Newborn Calf Serum

Serum of this category originates from 3 to 10 day old calves and contains a somewhat higher proportion of proteins and immunoglobulins, but fewer growth factors than Foetal Bovine Serum. It is nevertheless suitable for culturing most mammalian cell lines. Due to its lower price, it tends to be used in large batches, such as fermentation processes.

Product	Cat. No.	Volume
Neo-natal Foetal Bovine Serum		
USDA approved	A11-315	100 ml
	A15-315	500 ml
USDA approved, Heat Inactivated	A11-316	100 ml
	A15-316	500 ml
USDA approved, Gamma Irradiated	A11-317	100 ml
	A15-317	500 ml

Product	Cat. No.	Volume
Newborn Calf Serum		
USDA approved	B11-001	100 ml
	B15-001	500 ml
USDA approved, Heat Inactivated	B11-102	100 ml
	B15-102	500 ml
USDA approved, Gamma Irradiated	B11-303	100 ml
	B15-303	500 ml

Bovine Sera

The Alternative to FBS

Product	Cat. No.	Volume
Calf Serum	B11-004	100 ml
	B15-004	500 ml
Heat Inactivated	B11-106	100 ml
	B15-106	500 ml
Gamma Irradiated	B11-307	100 ml
	B15-307	500 ml

Product	Cat. No.	Volume
Donor Calf Serum	B11-008	100 ml
	B15-008	500 ml
Heat Inactivated	B11-109	100 ml
	B15-109	500 ml
Gamma Irradiated	B11-310	100 ml
	B15-310	500 ml

Product	Cat. No.	Volume
Bovine Serum	B11-011	100 ml
	B15-011	500 ml
Heat Inactivated	B11-112	100 ml
	B15-112	500 ml
Gamma Irradiated	B11-313	100 ml
	B15-313	500 ml

Product	Cat. No.	Volume
Donor Bovine Serum	B11-063	100 ml
	B15-063	500 ml
Heat Inactivated	B11-164	100 ml
	B15-164	500 ml
Gamma Irradiated	B11-365	100 ml
	B15-365	500 ml

Calf Serum

Calf Serum is obtained from animals which are not more than 12 months old and its protein content is approximately twice that of FBS. It is suitable for robust cell lines and short-term cell cultures, which do not need to be passaged many times, as it contains fewer growth factors than FBS or serum from newborn calves. Calf Serum is a lower cost alternative to FBS and is ideally suitable for fermentations. Furthermore it can act as a stabilizer in diagnostic assays, as a control standard or for isolating bovine proteins.

Donor Calf Serum

Donor Serum does not originate from slaughtered animals, but instead from donor calves from inspected herds. It is suitable for the same applications as conventional calf serum, but has a lower endotoxin content than serum from slaughtered animals and exhibits a lower level of batch-to-batch variation.

Bovine Serum

Serum of this category originates from cattle which are more than 12 months old. Bovine Sera have a low haemoglobin content. It is used not only as an addition to cell culture media, but also as a control standard and for many assays, for calibrating measurement methods or for reducing nonspecific reactions in ELISA.

Donor Bovine Serum

Donor Serum is obtained from donor animals and not from slaughtered animals. Advantages over conventional Bovine Serum from slaughtered animals are the lower endotoxin content and the lower level of batch-to-batch variation. Otherwise, it is used for the same applications.

Animal Sera

Species-specific

Horse Serum

Horse Serum has a higher protein concentration than FBS, but has a lower trace element content. It is thus often used as an additive for cell culture media which already contain these trace elements and has proved to be particularly suitable for culturing neuronal cells, haematopoietic stem cells, muscle cells and osteoblasts. Another significant area of application for Horse Sera are diagnostic methods and the multiplication of bovine-pathogenic viruses, which would be disrupted by the antibodies present in Bovine Serum. Horse haemoglobin has a different structure from bovine haemoglobin and rapidly breaks down to form bilirubin. Haemoglobin residues in Horse Sera may thus result in a green colouration, but this has no negative impact on the cells being cultured.

Donor Horse Serum

Donor Serum is obtained from donor animals and not from slaughtered animals. Advantages are the lower endotoxin content and the lower level of batch-to-batch variation. Otherwise, it is used for the same applications

Other Animal Sera

It is sometimes necessary for foreign proteins not to be introduced into cell culture systems. This is the case, for example, with autologous cell culturing because as few rejection reactions as possible should be caused when cultured cells are reimplanted into the test animal. PAA can thus supply animal sera for common test animal species. Another important area of application are immunohistological methods, such as immunofluorescence tests.

Porcine Serum is often used in cultures for multiplying mycoplasmas or viruses.

Goat and Sheep Serum are of particular use in immunohistochemistry and are often used to suppress nonspecific binding reactions. They are rarely used as a cell culture additive.

Product	Cat. No.	Volume
Horse Serum	B11-021	100 ml
	B15-021	500 ml
Heat Inactivated	B11-122	100 ml
	B15-122	500 ml

Product	Cat. No.	Volume
Donor Horse Serum	B11-023	100 ml
	B15-023	500 ml
Heat Inactivated	B11-124	100 ml
	B15-124	500 ml



Product	Cat. No.	Volume
Porcine Serum	B11-030	100 ml
	B15-030	500 ml
Sheep Serum	B11-032	100 ml
	B15-032	500 ml
Rabbit Serum	B11-034	100 ml
Goat Serum	B11-035	100 ml
	B15-035	500 ml
Rat Serum	B02-037	20 ml
	B11-037	100 ml
Mouse Serum	B02-038	20 ml
	B11-038	100 ml

Human Sera

The Human Factor



Human Serum in the culture medium provides human cell lines with an environment more closely matching their physiological conditions than media with animal sera. This is of particular significance in micro-optical investigations of cell structures or differentiation studies, whose results are intended to allow conclusions to be drawn regarding natural conditions in human tissue. Human serum may be superior to animal sera when culturing sensitive human cell lines. This particularly applies to immune cells such as macrophages or lymphocytes.

Human Serum is a highly sensitive material and is subject to the most stringent safety regulations. PAA's sera are obtained solely from donors from the USA. We work together with blood donation and plasmapheresis centres which meet the FDA's stringent requirements. The material (serum or whole blood) is obtained from donors who are HIV 1/2, HIV Ag, anti-HCV, HBsAg and RPR negative and have already been under medical supervision for at least 6 months. Each individual donation is subjected to extremely intensive testing with regard to various biophysical parameters and is tested for virus infections. The individual donations are combined into pools of 50 – 200 l, which are then sterile-filtered at a pore size of 0.2 μm . The osmolality and pH value of each batch of Human Serum is measured and sterility is checked. In addition, a low endotoxin value of ≤ 20 EU/ml is guaranteed and the biological activity and associated suitability for cell culture are checked in a toxicological cell test.

The entire process for the production of Human Serum complies with cGMP guidelines and is under permanent FDA control. All manufacturing steps and test results are accurately documented and can at all times be traced back to the individual donor by reference to the export certificate, production record, manufacturing report and certificate of analysis.

PAA can supply two different categories of Human Serum:

Converted Serum is produced from plasma (the cell-free supernatant of centrifuged blood), which is combined with citrate-phosphate-dextrose and then recentrifuged. It still contains all the clotting factors and its composition largely corresponds to the physiological conditions in blood. The addition of anticoagulants may, however, modify ion concentrations in the serum, which is disruptive in certain analytical methods.

Human Serum Off the clot is obtained by centrifuging blood which has passed through the natural clotting process. All clotting factors are absent, but the serum contains many thrombocyte constituents which may have a growth promoting action on cultured cells. Chemical conditions in the serum are strongly influenced by the biochemical processes which proceed during clotting and thus no longer correspond to the physiological conditions which prevail in blood. As a result, Human Serum Off the clot contains no unnatural additives.

Human Serum, Converted

This serum is collected in plasmapheresis centres. The addition of citrate-phosphate-dextrose converts fibrinogen into fibrin, which can then be removed by centrifugation. Converted Human Serum is suitable not only as an additive to culture media, but also for control assays, immunoassays, clinical chemistry and *in vitro* diagnostics.

PAA can also supply converted human serum originating exclusively from donors of blood group AB whose blood contains neither anti-A nor anti-B antibodies which can damage cultured human cells and disrupt immunological investigations.

Human Serum, Off the clot

Human Serum Off the clot is obtained from whole blood which has not been treated with anticoagulants. It goes through the natural blood clotting process and only then is it centrifuged, so removing the solid constituents of the blood together with the fibrin. It is particularly suitable for culturing human lymphocytes and macrophages.

This serum can also be supplied as type AB. It contains neither anti-A nor anti-B antibodies.

Product	Cat. No.	Volume
Human Serum, Converted		
	C11-001	100 ml
	C15-001	500 ml
Type AB	C11-002	100 ml
	C15-002	500 ml

Product	Cat. No.	Volume
Human Serum, Off the clot		
	C11-020	100 ml
	C15-020	500 ml
Type AB	C11-021	100 ml
	C15-021	500 ml



Sera | Practical Tips



Sera are highly complex biological materials. Their biological activity depends on many factors, which include correct handling during storage, freezing and thawing.

Since water freezes first during freezing and the ice floats to the surface due to its lower density, elevated concentrations of salt and other substances arise in the remaining liquid fraction. This can damage sensitive serum constituents. Rapid freezing minimizes these effects therefore all PAA sera are flash frozen after production.

Storage

PAA serum is supplied to you deep frozen in unbreakable PET bottles on dry ice in a polystyrene foam package. Any serum which you do not use straight away should be stored protected from light at $-15\text{ }^{\circ}\text{C}$ to $-40\text{ }^{\circ}\text{C}$. Partial thawing of the serum before it is placed in storage should be avoided.

Thawed serum should not be repeatedly frozen, but instead stored in the refrigerator at $2\text{ }^{\circ}\text{C}$ to $8\text{ }^{\circ}\text{C}$. If you only require small quantities of serum at a time, we would recommend freezing small aliquots which you can thaw and used as required.

Thawing

As with freezing, thawing of the sera should proceed as quickly as possible in order to minimize the period of time during which elevated salt concentrations prevail in the thawed liquid. The serum must not be exposed to elevated temperatures during thawing as sensitive molecules could be denatured. When bottles are taken from the freezer, they should be allowed to acclimatise for approximately 10 minutes at room temperature or overnight in the refrigerator. The sera may then be thawed in a water bath at $37\text{ }^{\circ}\text{C}$. Take care to ensure that the bottles do not float in the water and tip over. Frequent swirling of the serum is important during thawing as this disperses the released salts and proteins uniformly in the liquid and prevents some of the serum from being exposed to elevated temperatures for extended periods. Avoid repeated freeze-thaw cycles as precipitation may otherwise easily occur. The serum should also be swirled occasionally while working at room temperature in order to ensure that the liquid remains homogeneous.

Shelf Life

Serum may be stored $\leq -15\text{ }^{\circ}\text{C}$ to $-40\text{ }^{\circ}\text{C}$ for five years without any appreciable reduction in biological activity. Thawed serum can be stored without any problems for eight weeks at $2\text{ }^{\circ}\text{C}$ to $8\text{ }^{\circ}\text{C}$. More recent studies have shown that the activity of sera stored in this way has still undergone hardly any reduction even after 26 weeks.

Service

What can we do for you?



PAA offers much more than an extensive ordering and delivery service. On request, we are happy to supply samples of all our serum products for you to trial in your cell culture. If you have identified a batch of serum which is particularly suitable for your purposes, we can reserve a quantity of up to 2.600 litres. Depending on your requirements PAA will store your selected batch and deliver it to you at times and quantities of your choosing. On request, we can also supply your serum in special packaging other than the usual 100 ml and 500 ml containers. Just give us a call, we will be happy to advise you.



Our aim is not only to produce high quality products for your cell culture, but also to provide you with advice and practical assistance in your day to day scientific work. This is why PAA has a technical service team with the skills to provide you with further assistance in matters relating to cell culture.

Should you need further information relating to sera or other PAA products, precise details of their composition and physicochemical properties may be found in our main catalogue or on the internet at www.paa.com.

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