

## ***How is bovine serum produced and tested?***

Bovine blood that is to be processed to serum may be collected either from animals at the time of slaughter or from donor animals.

Fetal bovine blood and blood from animals that are kept in donor herds (see also: *What is bovine serum?*) is collected aseptically (i.e. using equipment designed to protect the material from microbial contamination) – just as is the case with human blood donation. These procedures are carefully monitored. The collection of fetal blood takes place in a specially provided area in the slaughterhouse/abattoir. Blood taken at slaughter from calves or adult cattle is collected under clean, controlled conditions.

The degree to which bovine serum is processed and tested depends to a significant extent upon the use to which it is to be put. What is vital, and is a commitment of the member companies of the ISIA, is that the sourcing, processing and testing are correctly performed, monitored and recorded and the serum consistently meets all relevant rules and regulations and the specific requirements of the customer.

Fetal bovine serum and (to a lesser extent) donor bovine serum are almost invariably used when serum is required for the manufacture of human pharmaceutical products. Veterinary vaccines, however, are often produced using other types of animal serum. Medicinal products must be produced following what is known as “Good Manufacturing Practices” (GMPs), a complex set of rules and requirements that are in place to ensure that the final product will be of the highest possible quality. GMPs impose obligations with regard to the raw materials that are used, like bovine serum, and these must be respected.

Let us take the manipulation of fetal bovine serum and donor bovine serum, destined for use in the manufacture of a pharmaceutical product, as examples of processing and testing.

The aseptically collected fetal or donor blood is refrigerated immediately after collection until coagulation is complete. The blood is then centrifuged to separate the serum from the blood clot and the serum is removed. The resultant serum is kept frozen in carefully identified clean, hygienic containers until it is thawed immediately prior to further processing. Serum, like many materials of biological origin, will deteriorate over time if it is not properly stored. In order to retain its properties it is stored and transported frozen. Great care is taken to ensure that the proper storage and transport conditions are maintained at all times.

A pre-defined quantity of serum is processed and tested at one time to form what is called a “batch” or “lot” of processed product. Processing of each batch is performed under controlled conditions by first thawing the designated material followed by “sterile filtration” which involves passing the material through a series of membrane filters with tiny pores that are of reducing size, the last of which will have a pore size that is small enough to remove and retain bacteria and fungi so that the serum is “sterile” (i.e. all

bacteria and fungi have been removed). The batch is frozen again immediately after filtration to preserve its quality.

Samples are comprehensively and carefully tested using approved tests (see also “*Is serum safe?*”) to confirm freedom from bacteria and other microorganisms. Extensive biochemical and biological testing are also performed. One important example: as certain microorganisms produce toxins that could be harmful and that would not be removed by filtration, the processed serum is carefully tested for such substances.

Viruses are not removed by sterile filtration. For this reason the batch must be tested to make sure that it is free from potentially contaminating viruses. As an additional safeguard (but not a replacement for testing) fetal bovine and donor serum is often gamma irradiated (gamma irradiation inactivates viruses) using controlled procedures in facilities specially validated for this purpose. Sterilization of the finished product by heat is not an option, as it would destroy many of the biologically active moieties necessary for cell growth.

Records are kept to ensure that each process step and the results of all testing performed can be linked directly to each individual batch of serum that is supplied to the customer. The customer may also perform tests on the batch prior to purchase and often these tests will be extensive. They are likely to include checks to confirm that the batch will perform optimally by promoting good growth of the customer’s specific cell lines of interest.

The overall testing process is very labour intensive and may take several months to complete.