International Serum Industry Association

Members of the International Serum industry Association are collectors, processors and users of animal serum and animal derived products. These products are used extensively in the growth of cells in culture for research and in the production of diagnostic kits, vaccines and bio-therapeutic molecules.

Mission Statement

ISIA shall 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. Our primary focus will be on safety and safe use of serum and animal derived products through proper origin, traceability, truth in labeling and appropriate standardization and oversight.

What is “serum”?

Serum is the liquid fraction of clotted blood. Bovine serum, the most extensively used animal serum, is a by-product of the meat industry. Bovine blood is collected at slaughter from cattle of all ages and from the fetuses of cows found to be pregnant at the time of slaughter.

It is also obtained from live adult “donor” animals, which give blood more than once. Serum from many other species is also collected, processed and is used in similar applications

Irrespective of whether blood is taken at slaughter or from donors, the age of the animal is an important consideration because it impacts on the characteristics of the serum. Bovine serum is categorized according to the age of the animal from which the blood was collected as follows:

- "Fetal bovine serum" comes from fetuses
- "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
- "Donor bovine serum" comes from Donor animals which can be up to three years old.

The processing of serum takes place under very tightly controlled conditions using sophisticated facilities and equipment, is accompanied by extensive testing and is subject to audit by government veterinary authorities.

Other animal derived products

Almost every part of an animal has value to many industries. A wide range of materials from antibodies to enzymes, extracts and actual animal parts are used in research and in the manufacturing of health-care related products. These materials are subject to the same levels of regulation as serum and hence have become part of the purview of the ISIA.

What are serum and other animal derived products used for?

Processed serum and other animal derived products are used in a wide range of applications. Perhaps the most important is in the field of pharmaceuticals where they are used in the research, manufacture and control of human and veterinary vaccines and of drugs ("biopharmaceuticals") many of which are at the cutting edge of drug development. Cell culture is a technique which is widely applied in the manufacture of both vaccines and biopharmaceuticals, and bovine serum in particular is extensively used in this application. Animal derived products are also critical components in the manufacture of in vitro diagnostic tests (IVDs).

Why use cell culture?

Cell culture is the process by which cells – human, animal or even insect – are grown under controlled conditions in vitro (outside the body). The possibility of maintaining animal tissues outside the body – at least for short periods of time – was demonstrated more than one hundred years ago. However, it was not until the 1940s and 1950s that the techniques were refined to produce cell cultures that could be used to cultivate viruses (which will only grow in living cells). This paved the way for the first virus vaccine to be produced using cell culture – polio vaccine, in 1955. The contribution to human and animal health of the vaccines that have resulted from the application of this technology is an ongoing global success story.

More recently, cell culture has been combined with what are called recombinant techniques to develop so-called recombinant-derived products ("biopharmaceuticals"). Whereas vaccines are almost invariably used to prevent disease these biopharmaceuticals offer important new opportunities for treatment and diagnosis. They are a hugely important and very rapidly expanding area of modern medicine.

Another significant and growing application of cell culture is in the safety testing of widely used products such as cosmetics and household chemicals. As the use of live animals for the safety testing of such products (cosmetics especially) has come increasingly under the political and ethical spotlight, cell culture technology has been used more and more to reduce or eliminate testing in animals.
Maintaining cells in vitro in a healthy condition and over time is a complex task. They will only survive, grow and multiply if they are well fed and provided with an appropriate and protective environment. Complex mixtures of substances ("media") are used to bathe the cells in order to both feed and protect them. Different cells have different requirements. In many instances the presence of serum in the mixture is essential if the cells are to grow adequately and normally. Bovine serum is much the most widely used, because high quality bovine serum is available in sufficient volume and has been found to support cell growth very well indeed. Other animal derived products also play a role in the successful culture of various cell lines.

So how can ISIA help you?
ISIA’s focus on the understanding of and discussion with regulatory authorities about regulations, as well as the focus on standardization and traceability, can provide significant support to your organization in these areas.

Regulations
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.

ISIA has played an active role in discussion with various regulatory bodies in the evolution of these and other regulations.

Guidance
The complexity of the regulations, particularly those of the European Union, covering, as they do, all animal by-products, from blood products, through bio-fuels, manure, pet food, milk and aquiculture, game animals etc, do not make for easy reading. Adding to the difficulty of easy interpretation are the many languages of the Union, and the incomplete harmonization of the application of these regulations by veterinary authorities at border inspection posts in the many nations comprising the Union.

In order to bring clarity to this situation, ISIA has worked with the European Diagnostic Manufacturers Association (EDMA) to produce a document which provides step-by-step guidance regarding the European animal by-products regulatory framework for suppliers, manufacturers, importers and other interested parties of medicinal products, veterinary medicinal products, medical devices, active implantable medical devices, in vitro diagnostic medical devices, and laboratory reagents.

The procedures and requirements described in the chapters of this document have been simplified to provide as clear guidance as possible, given the complexity of the animal by-products framework. This document is intended to provide guidance only and cannot replace an understanding of the legal framework: in all cases, please consult the legal texts laid down in Regulations (EC) No 1069/2009 and (EU) No 142/2011 and other derogations.

This guidance document reduces 350+ pages of legislation to 30 pages of industry specific information and provides ISIA members with:
- Technical guidance on which products fall within the scope of Regulation (EC) No 1069/2009 and which do not.
- Identification of the key provisions which are applicable to those products which fall within the scope of Regulation (EC) No 1069/2009.
- Technical mechanisms for compliance with the applicable provisions of Regulation (EC) No 1069/2009, in line with the recommendations within the implementing measures laid down in Regulation (EU) No 142/2011 and other derogations.

Quality Control
In line with the need to comply with the various regulations governing the activities of those in this industry, goes the need for rigorous quality management. This involves strictly structured and enforced SOPs, HAACP procedures, GMP etc. All facilities dealing with animal by-products and derived products are required to be registered by their national authority and are regularly audited to ensure compliance. Additionally, all client companies routinely conduct audits of their suppliers. ISIA has worked
closely with the United States Pharmacopeia to standardize QC testing and to develop a fetal bovine standard for use in ensuring growth assays are performed properly.

**Country of Origin**

The regulations mentioned above were initially driven by the outbreak of Mad Cow Disease in Britain in 1986 and dioxin contamination in Belgium in 1999. Since then, worldwide controls in the feeding, slaughter and sourcing of animals which are subject to this and related diseases has resulted in the virtual elimination of Bovine Spongiform Encephalitis (BSE) in the major cattle producing countries. The OIE recognizes the disease status of every nation for all animal diseases and categorizes these sources based on their risk factor. Knowledge of the country of origin is therefore critical and is a key component of the ISIA Traceability Program.

**Traceability**

A crucial element of such Quality Assurance and Control lies in Traceability. In other words, at any stage in the industrial process between “farm and fork” ie original source to end user, there must be a complete paper trail to guarantee that the end product contains exactly what it purports to contain, that its national and species origin is genuine as stated and that it has been processed and handled at all times according to stated protocols. The ISIA, as part of its core activity and raison d’être, has developed a Traceability Audit Program which member companies can elect to have conducted on their facilities by an independent auditor in order to establish, beyond doubt, that

- The serum or plasma they produce is traceable back to the collection facility and even back to the farm of origin.
- It is complete and unadulterated by any other sera or plasma from other than stated sources.

Member companies which pass this audit are selectively entitled to use the ISIA Quality Seal™, as proof of their having been successfully audited.

It is increasingly recognized by end users that sourcing their material from an ISIA traceability certified supplier is good manufacturing practice.

**Why be an ISIA member?**

ISIA has developed strong relationships with regulators and associations worldwide. As a member of ISIA, you will benefit from ISIA’s global connections and obtain relevant information at an early stage!

ISIA membership will help you make better and faster decisions, and save you time and resources. Your password protected entree to the members-only section of the website gives you easy access to a wide variety of information relating to ongoing and past ISIA activities and global regulations.

ISIA is proactive, holding regular meetings with regulatory groups and often receiving information prior to it being made available to the general public. Members receive continual updates, and are frequently asked for comments on regulations prior to their implementation, thus allowing specific concerns to be heard and addressed.

ISIA provides summaries of complex legislation for its members, developing guidance that can save you the time and costs associated with problem shipments. Due to ISIA’s continuous communication, our network of regulators can help resolve member issues quickly.

ISIA membership introduces you to a strong network, enabling you to exchange best practices and views on key issues of interest to our industry. You can volunteer for one of our regional committees and help to influence the future regulatory environment by sharing information, pooling resources and dealing with issues of common interest.

**Full Membership**

Full Membership is available to companies and groups actively engaged in the collection, sale, distribution, and processing of serum and animal derived products.

**Associate Membership**

Associate Membership is available to individuals, companies, universities, research institutions, government agencies and other organizations engaged in ancillary activities and in supportive functions but not actively engaged in the collection, sale, distribution, and processing of serum and animal derived products.