International Serum Industry Association	Doc. No.: TRC-SOP-POL-007	Rev.: 7	Effective Date: 15JAN2019
TITLE: Traceability Policy			

1.0 PURPOSE

The purpose of this policy is to provide International Serum Industry Association (ISIA) standards to ensure that the geographic origin and type of serum (species and age) represented on the product is, in fact, accurate, true, and traceable to the abattoir(s) or donor farm(s) where the raw blood was collected.

Animal serum is used in the manufacturing of vaccines, diagnostic tools and biologicals that are intended for use in humans and animals. Manufacturers of these products need to know the animal serum they use is safe. Animal serum is also used in the development of new drugs. All customers need to be able to trust that the serum they use is accurately described on the bottle label.

2.0 SCOPE

This procedure applies to member companies who desire to become ISIA traceability certified and all types of animal blood/serum they produce

3.0 ROLES AND RESPONSIBILITIES

Role	Responsible for
Board of Directors	• Review and approval of the traceability policy • Communication of policy to membership
Traceability Strategic Committee	• Providing recommendations for improvement of the program • Updating the traceability policy
ISIA Administrative Assistant	• Updating website with current version of the traceability policy
Chief Executive Officer (CEO)	• Provide feedback from the industry for improvement of the traceability policy
Compliant members	• Maintaining proper records as outlined in the traceability policy through one step forward of their position in the supply chain

4.0 REFERENCES

4.1 EC 1069/2009

4.2 EC 178/2002 This reference relates to FOOD regulations and is listed for information only

4.3 EC 1007/2006

4.4 EP 5.0; 5.2.8 Minimizing Risk of TSE

4.5 SANCO 10542/2006

5.0 DEFINITIONS / ABBREVIATIONS / ACRONYMS

Term	Definition
Whole Fresh Blood	Whole fresh blood is not modified, treated, or processed and contains no additives.
Whole Blood	Whole blood may contain anti-coagulants, but otherwise is not modified, treated or processed and contains no other additives.
Plasma	Plasma is the liquid fraction of un-clotted blood. After the addition of an anticoagulant to fresh whole blood, plasma is prepared by centrifuging the mixture until the red and white blood cells separate from the liquid phase. The plasma is then removed and may be stored frozen pending further processing.
Serum	Serum is the liquid fraction of clotted blood. It is depleted of cells, fibrin, and clotting factors. Serum differs from plasma in that anti-coagulant is never added to the blood after collection from the animal. Serum is prepared by centrifuging until the clot and remaining blood cells are separated from the liquid phase. The serum is then removed and stored frozen pending further processing.
Semi-processed Fetal Bovine Serum	Fetal bovine serum (FBS) is obtained as described above from the blood of fetuses of healthy, pre-partum bovine dams that have been deemed fit for human consumption through ante- and/or post-mortem veterinary inspection. It is collected in abattoirs inspected by the competent authority of the country of origin. Fetal blood is collected aseptically using cardiac puncture, thereby reducing the risk of microbial contamination and resultant endotoxins. Collection occurs in an area of the abattoir specifically set aside for this purpose to minimize the risk of contamination by other fluids. Fetal blood is allowed to clot and is then centrifuged. Semi-processed FBS is the liquid fraction of the clotted fetal blood. After separation by centrifugation, no further processing or treatment of the semi-processed FBS is allowed. Also, no additions (including preservatives) or deletions are allowed. Semi-processed FBS is stored frozen pending further processing.
Clarified Fetal Bovine Serum	Clarified FBS is semi-processed FBS, obtained as described above, that has been thawed, pooled, and subjected to some level of filtration before being dispensed into final packaging. No further processes, treatment, additions, or deletions are allowed. Clarified FBS is stored frozen pending further processing.

Term	Definition
Sterile Filtered Fetal Bovine Serum	Sterile filtered FBS is semi-processed FBS, obtained as described above, that has been thawed, pooled, and subjected to filtration (usually through a series of membrane filters culminating in a sterile 0.1-micron filter) before being aseptically dispensed into its final packaging, labeling, and placing on the market. No further processes, additions, or deletions are allowed. Sterile filtered FBS is stored frozen. Sterile filtered FBS may be treated using gamma irradiation or heat inactivation and additionally labeled to indicate the treatment method used.
Pre-Qualified or Screened Fetal Bovine Serum	This is sterile-filtered FBS that has been screened or qualified for suitability for a variety of specific applications. Examples may include Hybridoma screened, Stem Cell Screened, Insect Cell Screened, Low Endotoxin tested, or Low IgG tested. Pre-Qualified or Screened FBS may be labeled according to the application for which it has been qualified.
Specialty Fetal Bovine Serum	This is semi-processed FBS or sterile filtered FBS that has been subjected to one or more modification processes, or that has been enhanced or altered in any way. Examples are Dialyzed, Charcoal Stripped, IgG Stripped, pH Treated, Performance Enhanced, Dehydrated, and Reconstituted. Specialty FBS must be labeled in a manner that clearly identifies it as having been modified, enhanced, or altered and in what way(s).
Neo-natal Bovine Calf Serum	This serum is defined as the liquid fraction of clotted blood derived from newborn calves that have not suckled from the mother cow. It is collected in abattoirs inspected by the competent authority of the country of origin. There are no deletions or additions (including preservatives) allowed.
Newborn Calf Serum	Newborn Calf Serum (NBCS) is defined as the liquid fraction of clotted blood derived from healthy, slaughtered bovine calves aged less than 20 days, deemed fit for human consumption through ante- and/or post-mortem inspection. It is collected in abattoirs inspected by the competent authority of the country of origin. There are no deletions or additions (including preservatives) allowed.
Calf Serum	Bovine Calf Serum (BCS) is defined as the liquid fraction of clotted blood derived from healthy, slaughtered bovine calves, aged from 20 days up to 12 months, deemed fit for human consumption through ante- and/or post-mortem inspection. It is collected in abattoirs inspected by the competent authority of the country of origin. There are no deletions or additions (including preservatives) allowed.

Term	Definition
Donor Bovine Serum	Donor-sourced Bovine Serum (DBS) is defined as the liquid fraction of clotted blood derived from healthy cattle 12 months of age or older from controlled donor herds whose health status is confirmed by regular inspection by competent, legally authorized veterinarians. There are no deletions or additions (including preservatives) allowed.
Adult Bovine Serum Analog	Adult Bovine Serum Analog (ABSA) is defined as the product obtained by treatment of Adult Bovine Plasma by the addition of calcium and subsequent dialysis, or by freezing. Both methods result in clotting of fibrin and its removal. The plasma must be derived from healthy, slaughtered cattle 12 months of age or older, deemed to be fit for human consumption by anti- and/or post-mortem inspection. It is collected in abattoirs inspected by the competent authority of the country of origin.
Origin	The country where the animals were slaughtered or, in the case of donor animals, where the blood was collected. This includes animals born and raised in the country of origin, as well as imported animals, and may also include animals imported for immediate slaughter. (**Note:** We recognize that there could be differences between the serum and/or plasma industry definition of origin and standard trade or WTO definitions or rules about origin. In the best interest of the parties in ISIA we propose specific definitions for the origin of slaughterhouse derived materials and donor origin materials. Furthermore, we endorse the clear separation of batches of serum and/or plasma such that two or more origins of serum and/or plasma are not combined, or at least if they are combined then both origins appear on the official certification. See attachment 2 for further origin information.)

6.0 MATERIALS: Equipment and Supplies

N/A

7.0 PROCEDURE

7.1 This policy applies to **all** species and types of animal serum. When bovine serum is mentioned, a type of serum is required. Bovine types permitted are:

7.1.1 Fetal

7.1.2 Neonatal

7.1.3 Newborn

7.1.4 Calf

7.1.5 Adult

7.1.6 Donor

7.2 Each batch should ideally contain serum and/or plasma from only one origin. Exceptions to the one origin rule will be permitted provided the Certificate of Origin (CoO) and Certificate of Analysis (CoA) are clearly marked “Mixed Origin” and provide a list of each origin listed in order by volume from greatest to least. The batch number must appear on the certificate and link seamlessly and easily to all the abattoir/donor farm identification regardless of the country.

7.3 A CoO must be on official company letterhead and contain at least the following:

7.3.1 Species

7.3.2 Type of blood/serum/plasma

7.3.3 Origin – The origin is the country in which the animals were slaughtered, or the donor blood collected.

7.3.4 Each unique batch number represented by that certificate

7.3.5 Volume or weight of each unique batch number

7.3.6 Applicable health statements

7.3.7 Signature and date of an authorized employee

7.4 When two or more species or types of blood, serum, or plasma are combined, CoO and/or CoA must reflect that so each species and type of blood, serum, or plasma used to make the batch are clearly stated and listed in order by volume from greatest to least.

7.5 The conversion factor used to calculate volume from weight will be

7.5.1 Formalized within each organization

7.5.2 Scientifically sound

7.5.3 Clearly documented

7.6 All documents are to be maintained on file for a minimum of five years from the date of blood collection or the date of primary process pooling or date of final processing, depending on the date to which you have earliest access.

7.7 Blood Collection

7.7.1 An abattoir or donor farm log is to be maintained at each primary processing center for abattoirs/donor farms contributing blood supply to that center, and a master list of all supplying abattoirs/donor farms must be maintained at the member’s headquarters. For each abattoir/donor farm from which blood is received the log must contain:

7.7.1.1 Abattoir or donor farm name

7.7.1.2 Physical address

7.7.1.3 Telephone numbers

7.7.1.4 Name of the member's primary abattoir contact person

7.7.1.5 A unique identifying number. The number assigned by the National Agriculture Authority (NAA) is preferred. Where unique numbers are not provided by the NAA, the member must assign the unique numbers.

7.7.2 Each collection container is to be labeled with the blood type and species.

7.7.3 The invoice from the abattoir/donor farm will include:

7.7.3.1 Name of the collecting company

7.7.3.2 Number of liters or weight of blood collected

7.7.3.3 Price per liter or kilogram

7.7.3.4 Delivery docket number if dockets are used

7.7.3.5 Type of blood

7.7.3.6 Species

7.7.3.7 The time period represented by the invoice

7.7.3.8 Invoice or delivery docket number

7.8 Blood transfer – collection to primary processing plant (for remote, in-abattoir, or donor farm locations)

7.8.1 The shipping containers used to transport the blood are to be labeled with the following. If for some reason, the shipping containers cannot be labeled, the following should be easily found.

7.8.1.1 Type of blood

7.8.1.2 Species

7.8.2 A transfer document accompanies the shipment which certifies

7.8.2.1 Type of blood

7.8.2.2 Species

7.8.2.3 Number of containers

7.8.2.4 Abattoir number/donor farm name

7.8.2.5 Volume or weight of blood

7.8.2.6 Signature of (in order of preference) a NAA official, or an abattoir representative; or the collecting company representative.

7.9 Primary processing plant – blood processing to serum and/or plasma

7.9.1 A daily receiving log is to be maintained and must contain the following. Alternatively, the below information may be contained in the batch record.

7.9.1.1 Number of containers received

7.9.1.2 Date of receipt

7.9.1.3 Date of collection

7.9.1.4 Abattoir number/donor farm name

7.9.1.5 Volume or weight of each container

7.9.2 A daily processing log is to be maintained and must contain

7.9.2.1 Type of blood

7.9.2.2 Species

7.9.2.3 Volume of blood processed

7.9.2.4 Volume of serum/plasma produced

7.9.2.5 Country of origin

7.9.2.6 Abattoir identification number clearly linked to each pool or jug

7.9.2.7 Number of containers produced

7.9.3 The containers into which the serum/plasma is pooled for freezing must be labeled with

7.9.3.1 Type of serum/plasma

7.9.3.2 Species

7.9.3.3 Country of origin

7.9.3.4 Unique batch number

7.9.3.5 Unique continuous jug numbers within the batch

7.9.3.6 Name of company

7.10 Serum/Plasma transfer – primary processing plant to final processing plant

7.10.1 Each container is shipped labeled with

7.10.1.1 Type of serum/plasma

7.10.1.2 Species

7.10.1.3 Country of origin

7.10.1.4 Unique batch number

7.10.1.5 Unique continuous jug numbers within the batch

7.10.1.6 Name of company

7.10.2 Each shipment will be accompanied by a packing list/deliver note which contains

7.10.2.1 Type of serum/plasma

7.10.2.2 Species

7.10.2.3 Shipping date

7.10.2.4 Number of boxes

7.10.2.5 Unique batch numbers(s)

7.10.2.6 Number of jugs with a list of all the unique jug numbers

7.10.2.7 Volume of each jug

7.10.2.8 Country of origin

7.10.2.9 Name of company

7.11 Secondary processing plant – finishing of serum/plasma

7.11.1 A receiving log for each shipment received will contain

7.11.1.1 Whether or not a packing list accompanied the shipment

7.11.1.2 Number of boxes

7.11.1.3 Number of jugs

7.11.1.4 Volume of each jug

7.11.1.5 Shipper's name

7.11.1.6 Date received

7.11.1.7 Type of serum/plasma

7.11.1.8 Species

7.11.1.9 Country of origin

7.11.1.10 Batch number

7.11.1.11 Import permit number, if applicable

7.11.1.12 In addition, serum/plasma received from the donor farm will also have the following:

7.11.1.12.1 Donor farm name

7.11.1.12.2 Physical address

7.11.1.12.3 Telephone number

7.11.1.12.4 Name of the member's primary contact person at the farm

7.11.1.12.5 A unique identifying number

7.11.1.12.6 A copy of the Certificate of Registration of the farm from the NAA, if applicable

7.11.2 A daily processing log will be maintained for each batch and must contain the following. Alternatively, this may be included in the batch record.

7.11.2.1 Type of serum/plasma

7.11.2.2 Species

7.11.2.3 Batch number of finished product

7.11.2.4 Name of the supplier of the unfiltered product

7.11.2.5 Country of origin

7.11.2.6 Batch volume

7.11.3 A batch history record is to be maintained for each batch produced and will contain

7.11.3.1 Unique batch number

7.11.3.2 Type of serum/plasma

7.11.3.3 Species

7.11.3.4 Unfiltered, raw serum/plasma list containing

7.11.3.4.1 Number of containers used

7.11.3.4.2 Volume of each container

7.11.3.4.3 Batch number(s)

7.11.3.4.4 Country of origin including CoO accompanying the product

7.11.3.4.5 Name of the supplier(s)

7.11.3.5 CoA showing the results of the quality control tests and the country of origin

7.11.3.6 Finished product yield

7.11.3.7 QC testing data

7.11.3.8 Copies of finished product labels

7.11.3.9 CoO

7.11.4 Labels should be applied at the time of sterile filling. In rare occasions, filling into bottles with only the batch number may be permitted. Preferably, labels will be printed with the following information

7.11.4.1 Unique batch number

7.11.4.2 Container volume

7.11.4.3 Name of the owner

7.11.4.4 Owner contact information

7.11.4.5 Type of serum/plasma

7.11.4.6 Storage temperature

7.11.4.7 Expiration date

7.11.4.8 Origin – If a country of origin is not stated on the label, then it must be clearly stated on the CoO and CoA.

7.11.4.9 Use statement

7.12 Serum/plasma transfer – secondary processing plant to other locations

7.12.1 The origin must be clearly stated on the CoA and CoO along with the unique batch number

7.12.2 Each shipment will be accompanied by a packing list/deliver note which contains

7.12.2.1 Type of serum/plasma

7.12.2.2 Species

7.12.2.3 Shipping date

7.12.2.4 Number of boxes

7.12.2.5 Batch number(s)

7.12.2.6 Number of containers in each batch

7.12.2.7 Volume of containers

7.12.2.8 Name of company

7.13 Mergers and Acquisitions: In the event a certified company acquires a non-certified company, or a non-certified company acquires a certified company, the following apply:

7.13.1 The certification in place at the time of acquisition only applies to those products for which the processes have been certified through a successful ISIA traceability audit.

7.13.2 If the new entity wishes to maintain certification, a re-recertification plan must be submitted to the ISIA CEO. This re-certification plan will require an ISIA traceability audit to ensure new procedures do not interfere with current approved processes.

7.13.3 Recertification must occur within one year unless otherwise approved by the ISIA CEO.

7.14 Purchasing of Product

7.14.1 If a traceability certified member purchases finished product from a non-certified company, that material remains non-traceability certified, and the **ISIA-traceability seal cannot be used** in marketing material relating to that product, including, but not limited to, on letterhead, brochures, CoAs, etc.

7.14.2 If a traceability certified member purchases blood or raw serum from a non-certified company, the blood or raw serum is considered part of the

purchaser's quality system and therefore it is acceptable to use the ISIA-traceability seal if one of the following is true:

7.14.2.1 The independent Quality department of the purchaser has performed an audit that includes traceability and subsequently approved the source of the material.

7.14.2.2 The independent Quality department of the purchaser has provided an approved checklist, including traceability, to be used by trained personnel to evaluate the blood/raw serum supplier and the checklist has been satisfactorily completed and reviewed by Quality.

7.14.3 If a non-traceability certified member purchases product (raw or finished) from a traceability certified member, that material becomes non-traceability certified, and the **ISIA-traceability seal cannot be used** in marketing material relating to that product, including, but not limited to, on letterhead, brochures, CoAs, etc.

7.15 An independent, third-party audit will be used to test the integrity of the Traceability Policy at individual companies.

7.15.1 This audit is referred to as the ISIA Traceability Audit.

7.15.2 Member companies should notify the ISIA CEO that they are interested in certification and further directions will be given.

7.15.3 Auditors are approved by the ISIA CEO.

7.15.4 All records associated with the facility can be requested by the auditor. A company must have at least one year's work of records for the initial certification, which is granted for 3 years. Subsequent audits can cover all records generated in the last three years.

7.15.5 Findings

7.15.5.1 **Major Nonconformance** – A serious deficiency that could adversely affect the quality or cause doubts in traceability of product. These are required to be corrected to meet the established requirements of the traceability policy. Evidence of correction of the identified deficiency will be required to be reviewed and corrected prior to certification.

7.15.5.2 **Minor Nonconformance** – A temporary or isolated incident or a failure to comply with internal, regulatory procedures, specifications or requirements related to quality or established traceability requirements. A plan for the actions to be taken to satisfy these deficiencies with target dates must be submitted prior to certification.

Note: All identified nonconformance's, will be reviewed during the next audit to verify effectiveness of implementation of identified corrective actions.

7.15.5.3 **Opportunities for Improvement** – A situation or event that is not in violation of a procedure, specification or traceability requirement but considered to be poor practice. These events do not require an audit response or correction action plan and are noted on the report from.

8.0 ATTACHMENTS

8.1 Attachment 1: FBS Categories

8.2 Attachment 2: Origin Information

International Serum Industry Association	Doc. No.: TRC-SOP-POL-007	Rev.: 7	Effective Date: 15JAN2019

TITLE: Traceability Policy

Revision	Effective Date	Change Description	Originator
5		Policy in SOP format	Nicole Green
6	30AUG2018	-Add further definition to section 7.13.2 -Add definitions for audit findings and clear expectations for each type in 7.14.5	Nicole Green
7	01JAN2019	-Add clarification that the policy applies to all serum types -Add clarification that types are required for bovine serum -Add further definition to Purchasing of Product section -Add to Attachment 2 Origin Information	Nicole Green

ISIA	Doc. No.: TRC-SOP-POL-007	Rev.: 7	Effective Date: 15JAN2019
TITLE:	Traceability Policy – Attachment 1 FBS Categories		

Summary

Members should use the following categories for use preferably on labels but required in descriptions.

Categories

Natural FBS

Natural FBS represents normal pools of unfiltered and filtered FBS that have not been subject to any processes beyond normal collection.

Screened FBS

Screened FBS represents normal pools of FBS that have been screened by testing only to achieve various results. Examples: Low IgG FBS or Virus Free FBS

Treated FBS and Serum

Treated FBS and serum represents normal pools of serum that have undergone additional processes to achieve various results. Examples: Charcoal Treated, Heat Inactivated, Low IgG FBS or irradiated

Modified Serum

Modified serum represents normal pools of serum to which additional factors have been added. If the ISIA Seal is utilized, the associated product literature must state the seal applies only to the serum portion. Example: TurboCalf, Cosmic Calf

Alternative Serum

Alternative serum represents other types of serum that have been modified to simulate FBS. This may include newborn, calf serum of bovine serum with various additions. These products must describe the base serums used and the use of added enhancements. If the ISIA Seal is utilized, the associated product literature must state the seal applies only to the serum portion.

ISIA	Doc. No.: TRC-SOP-POL-007	Rev.: 7	Effective Date: 15JAN2019
TITLE:	Traceability Policy – Attachment 2 Origin Information		

Country of Collection – The country in which the animal was slaughtered, and the blood was collected or, in the case of donor animals, of collection only. (If a company is declaring an "Origin" on the label such as "Australian Origin" or "United States Origin" this should only apply to the country in which the blood was collected, and/or the animal was slaughtered.)

This is material sourced from registered authorities inspected by the competent veterinary authority in the country of collection. Some examples are below:

- Australia - Department of Water Resources (DAWR)
- Canada - Canadian Food Inspection Agency (CFIA)
- New Zealand - New Zealand Food Safety Authority (NZFSA)
- Mexico - Ministry of Agriculture, Livestock, Rural Development, Fisheries and Food (SAGARPA)
- United States – United States Department of Agriculture (USDA)

Country of Manufacture – This is the country in which the product was sterile filtered or clarified. Other acceptable terms include "Manufacturing Origin" or "Processed in". Note: the ISIA considers filtration to be a substantial transformation since pooled material cannot be unpooled. The term "manufacture" refers to the material, not the packaging.

Further Treatment – Treatments are performed in addition to sterile filtration or clarification such as gamma irradiation or heat inactivation. These can occur before or after sterile filtration and should be listed individually on the CoA or equivalent document. When treatments occur (i.e. before or after filtration) they should also be declared.

Country of Further Treatment – The country where the further treatment occurs. It is the recommendation of the ISIA that all member companies declare either on the label of a product or on the certificate of analysis all countries involved in the collection and processing of FBS. This includes any further treatment that is performed on the product.

Customs Origin – It is the view of the ISIA that a change of origin for Customs purposes does NOT impact the physical country of origin of a product. The physical origin (Country of Collection) of a product should be the origin reflected on all documentation including labels and Certificates of Analysis/Origin. It is, however, recognized that in certain circumstances, the Customs Origin of a product may change from one geography to another. A change in Customs origin may occur in the country where the material was last substantially transformed as defined by the regulating body in charge of the import/export of the product. What is considered a "substantial change" will vary among different controlled regulatory agencies. Customs origin should NOT be reported on a product label, CoA, or CoO.

USDA Grade

This material is sourced in countries approved for import into the United States by the USDA. While this is the case, this grade of material is NOT USDA approved – it is only approved for import and use from USDA approved countries. Currently, this includes Canada, Mexico, Panama, Costa Rica, El Salvador, Nicaragua, Honduras, Guatemala, Belize, Australia, New Zealand and Chile. This material is collected and processed in facilities registered and inspected by the competent veterinary authority in the country of origin. In many instances, the material cannot be distributed within the US without completion of USDA safety testing.

ISIA	Doc. No.: TRC-SOP-POL-007	Rev.: 7	Effective Date: 15JAN2019
TITLE:	Traceability Policy – Attachment 2 Origin Information		

EU Grade

This material is sourced in countries approved for import into the European Union by the European Commission. Currently, this includes countries from North, Central and South America, Australia, New Zealand and South Africa.