

European Directorate for the Quality of Medicines & HealthCare

Council of Europe



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European Directorate
for the Quality
of Medicines
& HealthCare | Direction européenne
de la qualité
du médicament
& soins de santé

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

Review of

European Pharmacopeia

requirements

for the use of **Bovine serum**

for the production of human and veterinary medicinal products

Catherine Lebrun, European Pharmacopoeia Department, EDQM

IABS-EU Meeting on Bovine Serum: challenges and opportunities in the research and development and manufacture of vaccines and other biological products, 29 September, 2026



Overview

- ★ The Council of Europe and the European Directorate for the Quality of Medicines & HealthCare (EDQM)
- ★ The bovine serum monograph: a bit of history
- ★ Content of the Bovine serum monograph (2262)
- ★ Work in progress on the monograph

European Directorate for the Quality of Medicines & HealthCare

★ Contributes to **public health and access to good quality medicines and healthcare in Europe**



The EDQM is a directorate of the Council of Europe

Council of Europe

Council of Europe

- ★ Established in **1949**
- ★ **46 member states**
- ★ Based in **Strasbourg**
- ★ Founded on three main values:
**human rights, democracy
and the rule of law**



**Convention on the Elaboration
of a European Pharmacopoeia
(ETS No. 050)**

July 1964

**European Convention for the
Protection of Vertebrate Animals
used for Experimental and other
Scientific Purposes (ETS No. 123)**

March 1986

EDQM

- ★ Founded in **1964**
- ★ Partial agreement (39 member states & the EU + 33 observers)
- ★ Contributes to **public health and access to good quality medicines and healthcare in Europe**
- ★ Wide scope of activities



Our vision

**Together for
better health,
for all**

Our mission

**To contribute to public health protection
by engaging with an international
community of experts and stakeholders**

EDQM, in Europe and beyond

Latest members:

Albania (2020), Republic of Moldova (2017).

Latest observers:

*Egypt (2023), Kyrgyz Republic (2023)
Ethiopia (2022), Mexico (2020),
Uzbekistan (2018), Japan (2016).*

The European Pharmacopoeia

European Pharmacopoeia members

European Pharmacopoeia observers

EDQM 39 member states & the EU

By [decision](#) of the Ministers' Deputies of 17 March 2022, the rights of representation of Belarus as observer in the European Pharmacopoeia Commission have been suspended.

By [decision](#) of the Ministers' Deputies of 1 June 2022, the rights of representation of the Russian Federation as observer in the European Pharmacopoeia Commission have been suspended.

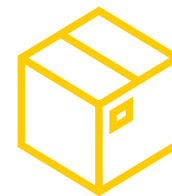
European Pharmacopoeia:

Documentary and reference standards

 Legally binding in the **40 signatory parties** of the Ph. Eur. Convention and used as a reference **worldwide**; **33 observers** from all continents

About **2 900 documentary standards** for the quality control of medicines

About **3 200 reference standards** shipped to **127 countries**



European Pharmacopoeia Commission and its **experts' groups**: global network of almost **1 000 experts**



PUBLIC HEALTH IMPACT

- Ensures quality and safety of medicinal products
- Facilitates their free movement in Europe and beyond



Ph. Eur.: Content and structure

Individual monographs

- Substance/product-based
- Specific but not stand-alone
- Based on approved specification(s) backed up by batch data

Bovine serum (2262)

General monographs

- Classes of substances/medicinal products
- Mandatory for all substances/preparations within their scope
- Not cross-referenced in individual monographs

Ex: *Substances for pharmaceutical use (2034)*,
Products with risk of transmitting agents of animal spongiform encephalopathies (1483)

Dosage form monographs

- Mandatory for all medicinal products of the type defined

General notices

- Apply to all texts
- Core principles for interpretation and application of Ph. Eur. texts

General chapters

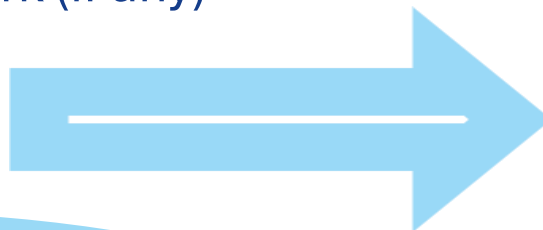
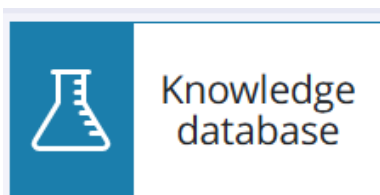
- Provide standard analytical procedures; guidance
- **Mandatory when referred to in a monograph**

Ex: 5.2.8. *Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products, Raw materials of biological origin for the production of cell-based and gene therapy medicinal products (5.2.12)*



The bovine serum monograph (2262): a bit of history

- In force since **1st April 2006 (Supplement 5.4)**
- *Scope*: from foetal to adult bovine serum (*Bos taurus* L.)
- Covers the quality for both **human and veterinary uses** (EU Guidelines)
- Consult EDQM knowledge database for the history of the text and the ongoing work (if any)



- Supplement 11.8 - Implementation 1st July 2025 - Revised for **Haemoglobin**: tightening the limit of 4 mg/mL to **0.5 mg/mL** to better reflect batch contents. No test method has been introduced.

Search Database online | Knowledge Database

edqm

Detailed view of Bovine serum.

Status	In use																
Monograph Number	02262																
English Name	Bovine serum																
French Name	Sérum bovin																
Latin Name	Serum bovinum																
Pinyin Name																	
Chinese Name																	
Pharmeuropa	19.1																
Last published in English	11.8																
Last published in French	11.8																
On-going	Revision																
State of work	1 - Draft																
Pharmeuropa																	
Description	General revision to reflect current practices																
Chromatogram	Not available																
Additional information	Not available																
History	View history																
Interchangeable (ICH_Q4B)	NO																
Pharmacopoeial harmonisation	NO																
Reference standards																	
Practical Information	<table><tr><th>Test(s)</th><th>Brand Name/Information</th></tr><tr><td>Monograph Number</td><td>Substance</td></tr><tr><td>2262</td><td>Bovine serum, (Product code B6683)</td></tr><tr><td>2262</td><td>Bovine serum</td></tr><tr><td>2262</td><td>Bovine serum</td></tr><tr><td>2262</td><td>Bovine serum</td></tr><tr><td>2262</td><td>Bovine serum, New Zealand origin</td></tr><tr><td>2262</td><td>Bovine serum, Iron-fortified</td></tr></table>	Test(s)	Brand Name/Information	Monograph Number	Substance	2262	Bovine serum, (Product code B6683)	2262	Bovine serum	2262	Bovine serum	2262	Bovine serum	2262	Bovine serum, New Zealand origin	2262	Bovine serum, Iron-fortified
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Type CEP	Certificate (CEP) Holder
TSE	Sigma-Aldrich Corporation Saint Louis US
TSE	JRH Biosciences Lenexa US
TSE	West Laboratories Inc Kankakee US
TSE	SERANA (WA) PTY. LTD. Bunbury AU
TSE	LIFE TECHNOLOGIES CORPORATION Carlsbad US
TSE	ATLAS BIOLOGICALS INC. Fort Collins US

Content of the Bovine serum monograph (2262) ⁽¹⁾

- Scope: from foetal to adult bovine serum (*Bos taurus* L.)

BOVINE SERUM

Serum bovinum

07/2025:2262

DEFINITION

Liquid fraction of blood obtained from the ox (*Bos taurus* L.) and from which cells, fibrin and clotting factors have been removed.

Different types of bovine serum are used:

- *adult bovine serum* obtained at slaughter from cattle that are declared fit for human consumption;
 - *calf serum* obtained at slaughter from animals, fit for human consumption, before the age of 12 months;
 - *new-born calf serum* obtained at slaughter from animals before the age of 20 days;
 - *foetal bovine serum* obtained from normal fetuses from dams fit for human consumption;
 - *donor bovine serum* obtained by repeated bleeding of donor animals from controlled donor herds.
- General quality specifications for bovine serum → reduce the risk of contamination for a safe use of bovine serum in the manufacture of medicinal products such as vaccines

*This monograph provides a general quality specification for bovine serum. Various measures are applied during the production of bovine serum aimed at obtaining a product that is acceptable as regards viral safety. No single measure, nor the combination of measures outlined below, can guarantee complete viral safety, but rather they reduce the risk involved in the use of serum in the manufacture of medicinal products. It is therefore necessary for the manufacturer of a medicinal product to take account of this when choosing the serum for a particular use by making a **risk assessment**.*

Content of the Bovine serum monograph (2262) ⁽²⁾



- Serum production performed within a suitable **QUALITY SYSTEM** (defined by the **General Notices**)

1.1.1.1 Quality systems

The quality standards represented by monographs are valid only where the articles in question are produced within the framework of a suitable quality system. The quality system must assure that the articles consistently meet the requirements of the Ph. Eur.

- **Traceability** of serum is maintained from the final container to the abattoir or to the herd of origin
- Source = controled donor herd → regular **veterinary examination** to ascertain the health status + **quarantine measures** during which the animals are observed and tested to establish that they are free from all agents and antibodies from which the donor herd is claimed to be free + additional agents. It is recommended that animals in the herd should not be vaccinated against bovine viral diarrhoea virus (BVDV).
- **Separation** of the serum from blood cells and clot done under conditions designed to minimise microbial contamination.
- Serum from a number of animals is **pooled** → one batch: ensure homogeneity and sterility or low bioburden
 - **Tests**: sterility/bioburden and general and specific tests for viral contaminants

Content of the Bovine serum monograph (2262) ⁽³⁾

- INACTIVATION of the serum using **validated** procedures with respect to a **suitable representative range of viruses** covering different types (enveloped, non-enveloped, DNA, RNA viruses) tailored to the inactivation/removal method used, and including **BVDV as model virus, used for demonstrating the robustness of the inactivation process**. Serum free from antibodies against BVDV is used in part or all of the validation studies.
- For bovine serum intended for use in **immunological veterinary medicinal products**, for inactivation by **gamma irradiation** a **minimum dose of 30 kGy** is applied, unless otherwise justified and authorised.
- Critical parameters established (list provided for gamma irradiation) and used in the validation study
- QUALITY CONTROL TESTS APPLIED TO EACH BATCH **prior** and post-treatment
 - *Composition.*



Composition. The content of a suitable selection of the following components is determined and shown to be within the expected range for the type of serum: cholesterol, α -, β - and γ -globulin, albumin, creatinine, bilirubin, glucose, serum aspartate transaminase (SAST, formerly serum glutamic-oxaloacetic transaminase (SGOT)), serum alanine transaminase (SALT, formerly serum glutamic-pyruvic transaminase (SGPT)), phosphorus, potassium, calcium, sodium and pH.

Content of the Bovine serum monograph (2262) ⁽⁴⁾

- QUALITY CONTROL TESTS APPLIED TO EACH BATCH **prior and post-treatment**
 - *Tests for viral contaminants **prior treatment**.*
 - Validated **general tests** = inoculation into at least 2 distinct suitable cell lines (1 of bovine origin)
 - Validated **specific tests** in view of the country of origin of the serum (WOAH health status) – *non exhaustive list*: bluetongue virus, bovine adenovirus, bovine parvovirus, bovine respiratory syncytial virus, bovine viral diarrhoea virus, rabies virus and reovirus. If inactivated, virus identified and amount below effective inactivation. If not, rejected.
 - test for **BVDV antibodies**: an acceptance criterion is established taking account of the **risk assessment**.
 - *Tests for viral contaminants **post-treatment**. If BVDV was detected before virus inactivation/removal*

If bovine viral diarrhoea virus was detected before virus inactivation/removal, the following test for bovine viral diarrhoea virus is carried out after virus inactivation/removal.

Test for bovine viral diarrhoea virus. A validated test for bovine viral diarrhoea virus is carried out, for example by inoculation into susceptible cell cultures, followed by not fewer than three subcultures and detection by immunostaining. No evidence of the presence of bovine viral diarrhoea virus is found.

- *Case of non-treated serum:*

For serum that is not to be subjected to a virus inactivation/removal procedure, if evidence of viral contamination is found in any of the tests described above, the serum is not acceptable.

Content of the Bovine serum monograph (2262) ⁽⁵⁾

IDENTIFICATION

- A. The electrophoretic pattern corresponds to that for serum and is consistent with the type (foetal or other) of bovine serum.
- B. Bovine origin is confirmed by a suitable immunochemical method (2.7.1).

TESTS

Osmolality (2.2.35): 280 mosmol/kg to 365 mosmol/kg for foetal bovine serum and 240 mosmol/kg to 340 mosmol/kg for other types.

Total protein (2.5.33): 30 mg/mL to 45 mg/mL for foetal bovine serum and minimum 35 mg/mL for other types.

Haemoglobin: maximum 0.5 mg/mL, determined by a validated method, such as spectrophotometry.

Bacterial endotoxins (2.6.14): less than 10 IU/mL for donor bovine serum, less than 25 IU/mL for foetal bovine serum, less than 100 IU/mL for other types.

Sterility (2.6.1). It complies with the test. Use 10 mL for each medium.

Mycoplasmas (2.6.7). It complies with the test.

STORAGE

Frozen at – 10 °C or below.

LABELLING (defined by the **General Notices**)

The label states:

- the type of serum;
- where applicable, that the serum has been inactivated and the inactivation method;
- where the serum has been inactivated by gamma irradiation, the target minimum dose of the irradiation procedure.

1.5.1.11 Labelling

In general, labelling of medicinal products is subject to supranational and national regulation and to international agreements.

The statements in the Labelling section are not therefore comprehensive. In addition, for the purposes of the Ph. Eur., only those statements that are necessary to demonstrate compliance or non-compliance with the monograph are mandatory. Any other labelling statements are included as recommendations.

When the term '*label*' is used in the Ph. Eur., the labelling statements may appear on the container, the package, a leaflet accompanying the package, or a certificate of analysis accompanying the article, as decided by the competent authority.

Work in progress on the monograph

- ★ Currently under revision to reflect current practices including, when appropriate, to:
 - ★ update the production and tests sections;
 - ★ re-consider the current limits;
 - ★ reflect upon the inclusion of new analytical methods;
 - ★ replace the test for identification by a more explicit test;
 - ★ review and update, if necessary, the list of extraneous agents.
- ★ Any information or submission of comments/proposals supported by data is welcome

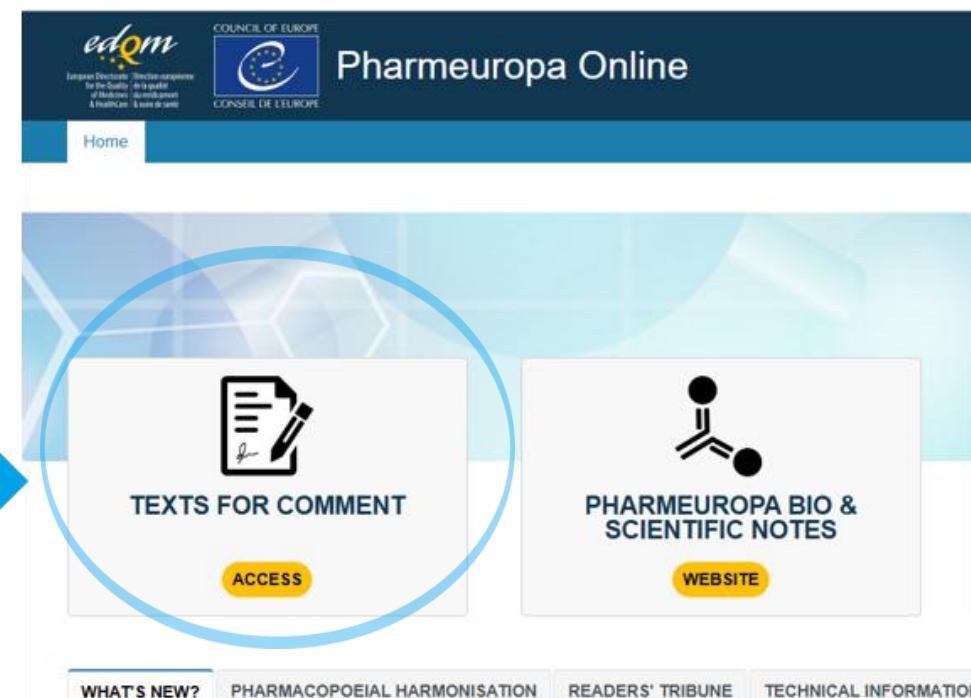
On 16/07/2024 [Call for experts – Join the Bovine Serum Working Party!](#)

7 experts nominated (2 from regul. Auth – 1 serum industry – 2 human vaccine manuf – 1 vet vaccine manuf – 1 US observer)

9 meetings/TC as of today.
2262 almost ready for public enquiry.

Watch the Pharmeuropa forum next year

Issue	Public commenting start	Public commenting end
39.1	01-01-2027	31-03-2027
39.2	01-04-2027	30-06-2027
39.3	01-07-2027	30-09-2027
39.4	01-10-2027	31-12-2027



Thank you for your attention!

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Backup slides

BOVINE SERUM

Serum bovinum

DEFINITION

Liquid fraction of blood obtained from the ox (*Bos taurus* L.) and from which cells, fibrin and clotting factors have been removed.

Different types of bovine serum are used:

- *adult bovine serum* obtained at slaughter from cattle that are declared fit for human consumption;
- *calf serum* obtained at slaughter from animals, fit for human consumption, before the age of 12 months;
- *new-born calf serum* obtained at slaughter from animals before the age of 20 days;
- *foetal bovine serum* obtained from normal fetuses from dams fit for human consumption;
- *donor bovine serum* obtained by repeated bleeding of donor animals from controlled donor herds.

This monograph provides a general quality specification for bovine serum. Various measures are applied during the production of bovine serum aimed at obtaining a product that is acceptable as regards viral safety. No single measure, nor the combination of measures outlined below, can guarantee complete viral safety, but rather they reduce the risk involved in the use of serum in the manufacture of medicinal products. It is therefore necessary for the manufacturer of a medicinal product to take account of this when choosing the serum for a particular use by making a risk assessment.

PRODUCTION

All stages of serum production are submitted to a suitable quality management system.

Traceability of serum is maintained from the final container to the abattoir of origin (for blood collected from slaughtered animals) or to the herd of origin (for blood collected from donor animals).

A further guarantee of the safety and quality of serum may be ensured by the use of a controlled donor herd. Where serum is obtained from such a herd, the animals are subjected to regular veterinary examination to ascertain their health status. Animals introduced into the herd are traceable as regards source, breeding and rearing history. The introduction of animals into the herd follows specified procedures, including defined quarantine measures. During the quarantine period the animals are observed and tested to establish that they are free from all agents and antibodies from which the donor herd is claimed to be free. It may be necessary to test the animals in quarantine for freedom from additional agents, depending on factors such as information available on their breeding and rearing history. It is recommended that animals in the herd should not be vaccinated against bovine viral diarrhoea virus. Tests are carried out for any agent and/or antibody from which the herd is claimed to be free.

Serum is obtained by separation of the serum from blood cells and clot under conditions designed to minimise microbial contamination. Serum from a number of animals is pooled and a batch number is allocated to the pool. Appropriate steps are taken to ensure homogeneity of the harvested material, intermediate pools and the final batch. Suitable measures (for example filtration) are taken to ensure sterility or a low bioburden. Before further processing, the serum is tested for sterility or bioburden. General and specific tests for viral contaminants are carried out as described below.

A step or steps for virus inactivation/removal are applied to serum intended for production of immunological veterinary medicinal products. Unless otherwise justified and authorised for a particular medicinal product, a step or steps for virus inactivation/removal are applied to serum intended for production of human and non-immunological veterinary medicinal products.

INACTIVATION

The inactivation procedure applied is validated with respect to a suitable representative range of viruses covering different types (enveloped, non-enveloped, DNA, RNA viruses). The optimal choice of relevant and model viruses depends strongly on the specific inactivation/removal procedure; representative viruses with different degrees of resistance to the type of treatment must be included. Bovine viral diarrhoea virus must be included in the viruses used for validation. Serum free from antibodies against bovine viral diarrhoea virus is used in part or all of the validation studies.

For bovine serum intended for use in immunological veterinary medicinal products, for inactivation by gamma irradiation a minimum dose of 30 kGy is applied, unless otherwise justified and authorised.

Critical parameters for the method of virus inactivation/removal are established and the parameters used in the validation study are strictly adhered to during subsequent application of the procedures to each batch of serum.

For inactivation by gamma irradiation, critical parameters include:

- the temperature;
- packaging configuration;
- distribution of dosimeters to assess the effective dose received by the product whatever its position;
- the minimum and maximum dose received.

QUALITY CONTROL TESTS APPLIED TO EACH BATCH

A suitable sample size for each batch is established. Specific tests for viral contaminants are validated with respect to sensitivity and specificity. The cell cultures used for general tests for viral contaminants are shown to be sensitive to a suitable range of potential contaminants. Control cells used in the tests are cultivated, where relevant, with a bovine serum controlled and inactivated as described in this monograph. Serum free from antibodies to bovine viral diarrhoea virus is required for validation of the effect of antibodies on the detection limits for bovine viral diarrhoea virus.

Tests carried out on the batch prior to treatment

The following tests are carried out on the serum (before any virus inactivation/removal steps, where applicable).

Tests for viral contaminants. General tests supplemented by specific tests are carried out.

General tests. Validated tests are carried out by inoculation of the serum on at least two distinct cell lines, one of which is of bovine origin. The cell lines used are suitable for detecting haemadsorbing viruses such as bovine parainfluenza virus 3 and cytopathic agents such as bovine herpesvirus 1.

Specific tests for viral contaminants (if not detected by general tests), where relevant in view of the country of origin of the serum: bluetongue virus, bovine adenovirus, bovine parvovirus, bovine respiratory syncytial virus, bovine viral diarrhoea virus, rabies virus and reovirus. Depending on the country of origin, specific tests for other viruses may be needed. The animal health status of countries is defined by the World Organisation for Animal Health (WOAH).

For serum that is to be subjected to a virus inactivation/removal procedure, if evidence of viral contamination is found in any of the tests described above, the serum is acceptable only if the virus is identified and shown to be present in an amount that has been shown in a validation study to be effectively inactivated.

For serum that is not to be subjected to a virus inactivation/removal procedure, if evidence of viral contamination is found in any of the tests described above, the serum is not acceptable.

A test for bovine viral diarrhoea virus antibodies is carried out; an acceptance criterion for the titre is established taking account of the risk assessment.

Composition. The content of a suitable selection of the following components is determined and shown to be within the expected range for the type of serum: cholesterol, α -, β - and γ -globulin, albumin, creatinine, bilirubin, glucose, serum aspartate transaminase (SAST, formerly serum glutamic-oxaloacetic transaminase (SGOT)), serum alanine transaminase (SALT, formerly serum glutamic-pyruvic transaminase (SGPT)), phosphorus, potassium, calcium, sodium and pH.

Tests carried out on the batch post-treatment

If bovine viral diarrhoea virus was detected before virus inactivation/removal, the following test for bovine viral diarrhoea virus is carried out after virus inactivation/removal.

Test for bovine viral diarrhoea virus. A validated test for bovine viral diarrhoea virus is carried out, for example by inoculation into susceptible cell cultures, followed by not fewer than three subcultures and detection by immunostaining. No evidence of the presence of bovine viral diarrhoea virus is found.

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