American National Standard

ANSI/AAMI/ ISO 22442-3:2007/ (R)2016

Medical devices utilizing animal tissues and their derivatives—Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents



Objectives and uses of AAMI standards and recommended practices

It is most important that the objectives and potential uses of an AAMI product standard or recommended practice are clearly understood. The objectives of AAMI's technical development program derive from AAMI's overall mission: the advancement of medical instrumentation. Essential to such advancement are (1) a continued increase in the safe and effective application of current technologies to patient care, and (2) the encouragement of new technologies. It is AAMI's view that standards and recommended practices can contribute significantly to the advancement of medical instrumentation, provided that they are drafted with attention to these objectives and provided that arbitrary and restrictive uses are avoided.

A voluntary standard for a medical device recommends to the manufacturer the information that should be provided with or on the product, basic safety and performance criteria that should be considered in qualifying the device for clinical use, and the measurement techniques that can be used to determine whether the device conforms with the safety and performance criteria and/or to compare the performance characteristics of different products. Some standards emphasize the information that should be provided with the device, including performance characteristics, instructions for use, warnings and precautions, and other data considered important in ensuring the safe and effective use of the device in the clinical environment. Recommending the disclosure of performance characteristics often necessitates the development of specialized test methods to facilitate uniformity in reporting; reaching consensus on these tests can represent a considerable part of committee work. When a drafting committee determines that clinical concerns warrant the establishment of minimum safety and performance criteria, referee tests must be provided and the reasons for establishing the criteria must be documented in the rationale.

A *recommended practice* provides guidelines for the use, care, and/or processing of a medical device or system. A recommended practice does not address device performance *per se*, but rather procedures and practices that will help ensure that a device is used safely and effectively and that its performance will be maintained.

Although a device standard is primarily directed to the manufacturer, it may also be of value to the potential purchaser or user of the device as a frame of reference for device evaluation. Similarly, even though a recommended practice is usually oriented towards healthcare professionals, it may be useful to the manufacturer in better understanding the environment in which a medical device will be used. Also, some recommended practices, while not addressing device performance criteria, provide guidelines to industrial personnel on such subjects as sterilization processing, methods of collecting data to establish safety and efficacy, human engineering, and other processing or evaluation techniques; such guidelines may be useful to health care professionals in understanding industrial practices.

In determining whether an AAMI standard or recommended practice is relevant to the specific needs of a potential user of the document, several important concepts must be recognized:

All AAMI standards and recommended practices are *voluntary* (unless, of course, they are adopted by government regulatory or procurement authorities). The application of a standard or recommended practice is solely within the discretion and professional judgment of the user of the document.

Each AAMI standard or recommended practice reflects the collective expertise of a committee of health care professionals and industrial representatives, whose work has been reviewed nationally (and sometimes internationally). As such, the consensus recommendations embodied in a standard or recommended practice are intended to respond to clinical needs and, ultimately, to help ensure patient safety. A standard or recommended practice is limited, however, in the sense that it responds generally to perceived risks and conditions that may not always be relevant to specific situations. A standard or recommended practice is an important *reference* in responsible decision-making, but it should never *replace* responsible decision-making.

Despite periodic review and revision (at least once every five years), a standard or recommended practice is necessarily a static document applied to a dynamic technology. Therefore, a standards user must carefully review the reasons why the document was initially developed and the specific rationale for each of its provisions. This review will reveal whether the document remains relevant to the specific needs of the user.

Particular care should be taken in applying a product standard to existing devices and equipment, and in applying a recommended practice to current procedures and practices. While observed or potential risks with existing equipment typically form the basis for the safety and performance criteria defined in a standard, professional judgment must be used in applying these criteria to existing equipment. No single source of information will serve to identify a particular product as "unsafe". A voluntary standard can be used as one resource, but the ultimate decision as to product safety and efficacy must take into account the specifics of its utilization and, of course, cost-benefit considerations. Similarly, a recommended practice should be analyzed in the context of the specific needs and resources of the individual institution or firm. Again, the rationale accompanying each AAMI standard and recommended practice is an excellent guide to the reasoning and data underlying its provision.

In summary, a standard or recommended practice is truly useful only when it is used in conjunction with other sources of information and policy guidance and in the context of professional experience and judgment.

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Medical devices utilizing animal tissues and their derivatives—Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents

Approved 24 January 2008 by Association for the Advancement of Medical Instrumentation

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Abstract: Specifies requirements for the validation of the elimination and/or inactivation of viruses and TSE agents during the manufacture of medical devices (excluding *in-vitro* diagnostic medical devices) utilizing animal tissue or products derived from animal tissue, which are non-viable or have been rendered non-viable. Does not cover other transmissible and non-transmissible agents.

Keywords: viruses, transmissible agents, TSE

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Glossary of equivalent standards

International Standards adopted in the United States may include normative references to other International Standards. For each International Standard that has been adopted by AAMI (and ANSI), the table below gives the corresponding U.S. designation and level of equivalency to the International Standard. NOTE: Documents are sorted by international designation.

Other normatively referenced International Standards may be under consideration for U.S. adoption by AAMI; therefore, this list should not be considered exhaustive.

International designation	U.S. designation	Equivalency
IEC 60601-1:2005	ANSI/AAMI ES60601-1:2005	Major technical variations
IEC 60601-1-2:2007	ANSI/AAMI/IEC 60601-1-2:2007	Identical
IEC 60601-2-2:2006	ANSI/AAMI/IEC 60601-2-2:2006	Identical
IEC 60601-2-4:2002	ANSI/AAMI DF80:2003	Major technical variations
IEC 60601-2-19:1990 and Amendment 1:1996	ANSI/AAMI II36:2004	Major technical variations
IEC 60601-2-20:1990 and Amendment 1:1996	ANSI/AAMI II51:2004	Major technical variations
IEC 60601-2-21:1994 and Amendment 1:1996	ANSI/AAMI/IEC 60601-2-21 and Amendment 1:2000 (consolidated texts)	Identical
IEC 60601-2-24:1998	ANSI/AAMI ID26:2004	Major technical variations
IEC 60601-2-47:2001	ANSI/AAMI EC38:2007	Major technical variations
IEC 60601-2-50:2001	ANSI/AAMI/IEC 60601-2-50:2006	Identical
IEC/TR 60878:2003	ANSI/AAMI/IEC TIR60878:2003	Identical
IEC/TR 62296:2003	ANSI/AAMI/IEC TIR62296:2003	Identical
IEC 62304:2006	ANSI/AAMI/IEC 62304:2006	Identical
IEC/TR 62348:2006	ANSI/AAMI/IEC TIR62348:2006	Identical
ISO 5840:2005	ANSI/AAMI/ISO 5840:2005	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001/(R)2004	Identical
ISO 7199:1996	ANSI/AAMI/ISO 7199:1996/(R)2002	Identical
ISO 8637:2004	ANSI/AAMI RD16:2007	Major technical variations
ISO 8638:2004	ANSI/AAMI RD17:2007	Major technical variations
ISO 10993-1:2003	ANSI/AAMI/ISO 10993-1:2003	Identical
ISO 10993-2:2006	ANSI/AAMI/ISO 10993-2:2006	Identical
ISO 10993-3:2003	ANSI/AAMI/ISO 10993-3:2003	Identical
ISO 10993-4:2002 and Amendment 1:2006	ANSI/AAMI/ISO 10993-4:2002 and Amendment 1:2006	Identical
ISO 10993-5:1999	ANSI/AAMI/ISO 10993-5:1999	Identical
ISO 10993-6:2007	ANSI/AAMI/ISO 10993-6:2007	Identical
ISO 10993-7:1995	ANSI/AAMI/ISO 10993-7:1995/(R)2001	Identical
ISO 10993-9:1999	ANSI/AAMI/ISO 10993-9:1999/(R)2005	Identical
ISO 10993-10:2002 and Amendment	ANSI/AAMI BE78:2002	Minor technical variations
1:2006	ANSI/AAMI BE78:2002/A1:2006	Identical
ISO 10993-11:2006	ANSI/AAMI/ISO 10993-11:2006	Identical
ISO 10993-12:2007	ANSI/AAMI/ISO 10993-12:2007	Identical
ISO 10993-13:1998	ANSI/AAMI/ISO 10993-13:1999/(R)2004	Identical
ISO 10993-14:2001	ANSI/AAMI/ISO 10993-14:2001/(R)2006	Identical
ISO 10993-15:2000	ANSI/AAMI/ISO 10993-15:2000/(R)2006	Identical
ISO 10993-16:1997	ANSI/AAMI/ISO 10993-16:1997/(R)2003	Identical

International designation	U.S. designation	Equivalency
ISO 10993-17:2002	ANSI/AAMI/ISO 10993-17:2002	Identical
ISO 10993-18:2005	ANSI/AAMI BE83:2006	Major technical variations
ISO/TS 10993-19:2006	ANSI/AAMI/ISO TIR10993-19:2006	Identical
ISO/TS 10993-20:2006	ANSI/AAMI/ISO TIR10993-20:2006	Identical
ISO 11135-1:2007	ANSI/AAMI/ISO 11135-1:2007	Identical
ISO 11137-1:2006	ANSI/AAMI/ISO 11137-1:2006	Identical
ISO 11137-2:2006 (2006-08-01	ANSI/AAMI/ISO 11137-2:2006	Identical
corrected version)		
ISO 11137-3:2006	ANSI/AAMI/ISO 11137-3:2006	Identical
ISO 11138-1: 2006	ANSI/AAMI/ISO 11138-1:2006	Identical
ISO 11138-2: 2006	ANSI/AAMI/ISO 11138-2:2006	Identical
ISO 11138-3: 2006	ANSI/AAMI/ISO 11138-3:2006	Identical
ISO 11138-4: 2006	ANSI/AAMI/ISO 11138-4:2006	Identical
ISO 11138-5: 2006	ANSI/AAMI/ISO 11138-5:2006	Identical
ISO/TS 11139:2006	ANSI/AAMI/ISO 11139:2006	Identical
ISO 11140-1:2005	ANSI/AAMI/ISO 11140-1:2005	Identical
ISO 11140-3:2007	ANSI/AAMI/ISO 11140-3:2007	Identical
ISO 11140-4:2007	ANSI/AAMI/ISO 11140-4:2007	Identical
ISO 11140-5:2007	ANSI/AAMI/ISO 11140-5:2007	Identical
ISO 11607-1:2006	ANSI/AAMI/ISO 11607-1:2006	Identical
ISO 11607-2:2006	ANSI/AAMI/ISO 11607-2:2006	Identical
ISO 11737-1: 2006	ANSI/AAMI/ISO 11737-1:2006	Identical
ISO 11737-2:1998	ANSI/AAMI/ISO 11737-2:1998	Identical
ISO 11737-3:2004	ANSI/AAMI/ISO 11737-3:2004	Identical
ISO 13485:2003	ANSI/AAMI/ISO 13485:2003	Identical
ISO 14155-1:2003	ANSI/AAMI/ISO 14155-1:2003	Identical
ISO 14155-2:2003	ANSI/AAMI/ISO 14155-2:2003	Identical
ISO 14160:1998	ANSI/AAMI/ISO 14160:1998	Identical
ISO 14161:2000	ANSI/AAMI/ISO 14161:2000	Identical
ISO 14937:2000	ANSI/AAMI/ISO 14937:2000	Identical
ISO/TR 14969:2004	ANSI/AAMI/ISO TIR14969:2004	Identical
ISO 14971:2007	ANSI/AAMI/ISO 14971:2007	Identical
ISO 15223-1:2007	ANSI/AAMI/ISO 15223-1:2007	Identical
ISO 15225:2000 and A1:2004	ANSI/AAMI/ISO 15225:2000/(R)2006 and A1:2004/(R)2006	Identical
ISO 15674:2001	ANSI/AAMI/ISO 15674:2001	Identical
ISO 15675:2001	ANSI/AAMI/ISO 15675:2001	Identical
ISO 15882:2003	ANSI/AAMI/ISO 15882:2003	Identical
ISO/TR 16142:2006	ANSI/AAMI/ISO TIR16142:2005	Identical
ISO 17664:2004	ANSI/AAMI ST81:2004	Major technical variations
ISO 17665-1:2006	ANSI/AAMI/ISO 17665-1:2006	Identical
ISO 18472:2006	ANSI/AAMI/ISO 18472:2006	Identical
ISO/TS 19218:2005	ANSI/AAMI/ISO 19218:2005	Identical
ISO 22442-1:2007	ANSI/AAMI/ISO 22442-1:2007	Identical
ISO 22442-2:2007	ANSI/AAMI/ISO 22442-2:2007	Identical
ISO 22442-3:2007	ANSI/AAMI/ISO 22442-3:2007	Identical
ISO 25539-1:2003 and A1:2005	ANSI/AAMI/ISO 25539-1:2003 and A1:2005	Identical

Committee representation

Association for the Advancement of Medical Instrumentation

Tissue Product Safety Committee

The adoption of ISO 22442-3:2007 as an AAMI standard was initiated by the Tissue Product Safety Committee (AAMI/TS), which also functions as a U.S. Technical Advisory Group to the relevant work in the International Organization for Standardization (ISO). U.S. representatives from the AAMI/TS, chaired by Richard Hutchinson and Donald E. Marlowe, played an active part in developing the ISO Standard.

Approval of this standard does not necessarily imply that all committee members voted for its approval.

At the time this document was published, the **AAMI Tissue Product Safety Committee** had the following members:

- Cochairs Richard W. Hutchinson, DVM PhD DABT, Johnson & Johnson Donald E. Marlowe, FDA/CDRH Joseph Carraway, DVM, NAMSA **Members** Kimbrell Darnell, CR Bard Gary S. Fischman, PhD, National Academies (Independent Expert) Frank A. Gomez, Abbott Charles Oren Hancock, RAC, H&W Technology LLC Mark E. Himes, Medtronic Inc. Joseph V Hughes, AppTec Richard W. Hutchinson, DVM PhD DABT, Johnson & Johnson Anita Kore, DVM,PhD, 3M Healthcare Christine Loshbaugh, Edwards LifeSciences Angela Mallery, St Jude Medical Inc. Donald E. Marlowe, FDA/CDRH Yukihiko Nose, MD PhD, Baylor College of Medicine (Independent Expert) Susan J. Schniepp, Hospira Worldwide Inc. Nancy J. Stark, PhD, Clinical Device Group Inc. Alternates Stephanie Board, St Jude Medical Inc
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NOTE—Participation by federal agency representatives in the development of this document does not constitute endorsement by the federal government or any of its agencies.

Background of AAMI Adoption of ISO 22442-3:2007

The International Organization for Standardization (ISO) is a worldwide federation of national standards bodies. The United States is one of the ISO members that took an active role in the development of this standard. ISO 22442-3 was developed by ISO Technical Committee 194, Subcommittee 1, to fill a need for an international standard for utilization of animal tissues and their derivatives in medical devices. The standard is part of a three-part series under the general title *Medical Devices Utilizing Animal Tissues and Their Derivatives*. The three parts are:

- Part 1: Application of risk management
- Part 2: Controls on sourcing, collection and handling
- Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents

These standards were developed in response to increasing concern about the spread of infectious diseases through the use of animal tissues in medical devices. Concurrent with the development of the U.S. position on the ISO 22442 series, the AAMI Tissue Product Safety Committee (AAMI/TS) also considered adopting the three parts verbatim, due to their relevance in the United States.

U.S. participation in ISO/TC 194/SC 1 is organized through the U.S. Technical Advisory Group to ISO/TC 194/SC 1, administered by the Association for the Advancement of Medical Instrumentation. The United States made a considerable contribution to this standard.

As used within the context of this standard, "shall" indicates requirements to be followed strictly in order to conform to the standard; "should" indicates that among several possibilities, one is recommended as particularly suitable, without mentioning or excluding others, that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action is undesirable but not prohibited; "may" is used to indicate that a course of action is permissible within the limits of the standard; "can" is used as a statement of possibility and capability; "must" is used only for those situations which cannot be otherwise, as in the example "Monday must follow Sunday."

AAMI (and ANSI) have adopted other ISO documents. See the Glossary of Equivalent Standards for a list of ISO standards adopted by AAMI, which gives the corresponding U.S. designation and the level of equivalency with the ISO standard.

AAMI and ANSI procedures require that standards be reviewed every five years and, if necessary, revised to reflect technological advances that may have occurred since publication.

The concepts incorporated in this standard should not be considered inflexible or static. This standard, like any other, must be reviewed and updated periodically to assimilate progressive technological developments. To remain relevant, it must be modified as technological advances are made and as new data comes to light.

Suggestions for improving this standard are invited. Comments should be sent to AAMI, Attn: Standards Department, 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795.

NOTE—Beginning with the ISO foreword on page "ix", this American National Standard is identical to ISO 22442-3:2007.

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 22442-3 was prepared by Technical Committee ISO/TC 194, *Biological evaluation of medical devices*, Subcommittee SC 1, *Tissue product safety*.

ISO 22442 consists of the following parts, under the general title *Medical devices utilizing animal tissues and their derivatives*:

- Part 1: Application of risk management
- Part 2: Controls on sourcing, collection and handling
- Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents

Introduction

Certain medical devices utilize materials of animal origin.

Animal tissues and their derivatives are used in the design and manufacture of medical devices to provide performance characteristics that were chosen for advantages over non-animal based materials. The range and quantities of materials of animal origin in medical devices vary. These materials can comprise a major part of the device (e.g. bovine/porcine heart valves, bone substitutes for use in dental or orthopaedic applications, haemostatic devices), can be a product coating or impregnation (e.g. collagen, gelatine, heparin), or can be used in the device manufacturing process (e.g. tallow derivatives such as oleates and stearates, foetal calf serum, enzymes, culture media).

It is important to be aware that the exposure to a properly validated and accurately controlled method of viral and TSE inactivation/elimination is not the only factor associated with demonstrating product safety. Attention has also to be given to a number of factors including sourcing, collecting, handling, storage, processing, testing of tissues and/or cells of animal origin, and to the control of the environment in which the product is manufactured, assembled and packaged. The manufacturer should consider the fact that each manufacturing phase can contribute to contamination as well as elimination and/or inactivation of viruses and TSE agents.

For the safety of medical devices there are two complementary approaches (see ISO 22442-1) that can be adopted to control the potential contamination of tissues. These typically are:

- a) selecting source material for minimal contamination with viruses and/or TSE agents (see ISO 22442-1 and ISO 22442-2);
- b) providing valid scientific evidence to demonstrate the ability of the production processes to eliminate or inactivate viruses and/or TSE agents (this part of ISO 22442).

Requirements for a quality system for medical devices for regulatory use are specified in ISO 13485. The standards for quality management systems recognize that, for certain processes used in manufacturing, the effectiveness of that process cannot be fully verified by subsequent inspection and testing of the product. The elimination and/or inactivation of viruses and TSE agents is an example of a special process because process efficacy cannot be verified by inspection and testing of the product. For this reason, the following need to be considered in particular:

- definition of the process(es) and materials to be used;
- adequate inactivation validation before routine use;
- performance monitoring of the process during manufacture;
- appropriate equipment maintenance;
- staff training, etc.

Historically there have been many instances of unknown or unsuspected viral contamination during manufacture. For this reason, evaluation of the manufacturing process can provide a measure of confidence that a wide number of viruses, including unknown pathogenic viruses are eliminated. Similar principles may apply to TSE agents.

NOTE To show compliance with this part of ISO 22442, its specified requirements should be fulfilled. The guidance given in the Notes and informative annexes is not normative and is not provided as a checklist for auditors.

Medical devices utilizing animal tissues and their derivatives — Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents

1 Scope

This part of ISO 22442 specifies requirements for the validation of the elimination and/or inactivation of viruses and TSE agents during the manufacture of medical devices (excluding *in vitro* diagnostic medical devices) utilizing animal tissue or products derived from animal tissue, which are non-viable or have been rendered non-viable. It applies where required by the risk management process as described in ISO 22442-1. It does not cover other transmissible and non-transmissible agents.

NOTE 1 Analysis and management of risk is described in ISO 22442-1. Conventional processes used for sterilization, when used for the treatment of animal tissues for medical devices, have not been shown to be completely effective in inactivating the causative agents of transmissible spongiform encephalopathy. Selective sourcing is extremely important (see ISO 22442-1 and ISO 22442-2).

NOTE 2 ISO 11135, ISO 11137, ISO 11737-1, ISO 13408, ISO 14160, ISO 14937 and ISO 17665 may be relevant for bacteria, moulds and yeast (see Bibliography).

This part of ISO 22442 does not cover the utilization of human tissues in medical devices.

This part of ISO 22442 does not specify a quality management system for the control of all stages of production of medical devices.

NOTE 3 It is not a requirement of this part of ISO 22442 to have a full quality management system during manufacture, but it does specify requirements for some of the elements of a quality management system. Attention is drawn to the standards for quality management systems (see ISO 13485) that control all stages of production or reprocessing of medical devices. The quality management system elements that are required by this part of ISO 22442 can form part of a quality management system conforming to ISO 13485.

This part of ISO 22442 does not consider the effect of any method of elimination and/or inactivation on the suitability of the medical device for its intended use.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 22442-1:2007, Medical devices utilizing animal tissues and their derivatives — Part 1: Application of risk management

ISO 22442-2, Medical devices utilizing animal tissues and their derivatives — Part 2: Controls on sourcing, collection and handling

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 22442-1 and the following apply.

3.1

model TSE agent

TSE agent that displays a known resistance to physical and/or chemical processing used as reference by analogy for the inactivation of relevant TSE agents, and thereby demonstrating the effectiveness of the process used for inactivation

3.2

model virus

virus that displays a known resistance to physical and/or chemical processing used as reference by analogy for the inactivation of relevant viruses, and thereby demonstrating the effectiveness of the process used for inactivation

NOTE This includes viral models (RNA, DNA, enveloped, non-enveloped) and bacteriophage models.

3.3

overall reduction factor

sum of the reduction factors of the individual process steps

3.4

permissive cell

cell that can become infected with the virus under study and in which that virus replicates

3.5

reduction factor

ratio of the virus or TSE agent load in the relevant material used or the device prior to the inactivation or elimination step and the virus or TSE agent load after the inactivation or elimination step when it is ready for the next step in the manufacturing process, expressed as the number of ten fold reduction (log₁₀)

3.6

relevant TSE agent

TSE agent known to, or likely to, contaminate the source material or other materials used in the manufacturing process

3.7

relevant virus

virus known to, or likely to, contaminate the source material or other materials used in the manufacturing process

3.8

revalidation

set of documented procedures to confirm an established validation

3.9

scaled down process

scaling down

process at a specified reduced scale which simulates the performance parameters as used in the full scale production process

3.10

sterilization

validated process used to render a product free of all forms of viable microorganisms

3.11

validation

documented procedure for obtaining, recording and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications

[ISO/TS 11139:2006, definition 2.55]

4 General requirements

4.1 Risk management

Analysis and management of risk shall be carried out in accordance with ISO 22442-1.

Due account shall be taken of manufacturing processes that are considered to be effective for certain animal materials as discussed in Annex C of ISO 22442-1:2007.

4.2 Sourcing and manufacturing process

A documented system shall be established and maintained to control the source of raw materials of animal origin. ISO 22442-2 shall be used to meet this requirement as far as applicable.

The manufacturing process shall be established to minimize the load of viruses and TSE agents in starting materials, intermediate products and finished products.

Appropriate documented protocols and procedures shall be established to ensure that the validated processing parameters will be applied during the routine manufacturing processes.

NOTE Employing a quality management system complying with ISO 13485 could be used to meet the requirements of this subclause.

4.3 General requirements related to validation

4.3.1 Documented procedures

The documented procedures and requirements of this part of ISO 22442 shall be implemented. Documentation and records shall be reviewed and approved by designated personnel (see 4.3.2).

Procedures for any literature review and/or any inactivation study shall be documented and records shall be retained for a period defined by the manufacturer.

4.3.2 Personnel

Responsibility for the implementation of this part of ISO 22442 shall be assigned to qualified personnel.

The requirements for the qualification, training or experience of personnel shall be documented and appropriate to the individual's work, responsibility and authority.

NOTE The level of qualification, training and experience required by personnel at various levels depends upon the activities being performed.