

L.N. 27 of 2004**PRODUCT SAFETY ACT
(ACT NO. V OF 2001)****Medical Devices (Amendment) Regulations, 2004**

IN exercise of the powers conferred by articles 38 to 40 of the Product Safety Act, the Minister of Finance and Economic Affairs, on the advice of the Malta Standards Authority, has made the following regulations:-

1. (1) The title of these regulations is Medical Devices (Amendment) Regulations, 2004, and they shall be read and construed as one with the Medical Devices Regulations, 2003, hereinafter referred to as “the principal regulations”. Citation and commencement.
L.N. 47 of 2003.

(2) These regulations shall come into force on the date of their publication:

Provided that the provisions of the following regulations shall enter into force on 1st April 2004:

- item 1.2.2 in regulation 2 of these regulations;
- items 3.1.23 to 3.1.34 in regulation 4 of these regulations; and
- regulations 5, 6, 7 and 8 of these regulations.

2. Immediately after regulation 1.2.1 of the principal regulations, there shall be inserted the following regulations: Amends regulation 1 of the principal regulations.

“1.2.2. Holders of EC design-examination certificates or EC type-examination certificates issued before 1st April 2004 for medical devices referred to in Article 1(1) of Directive 2003/32 shall apply for a complementary EC design-examination certificate or EC type-examination certificate attesting to compliance with the specifications laid down in Schedule XIII to these regulations.

1.2.3. Breast implants placed on the market before 1st September, 2003 pursuant to regulation 8.3(a) or regulation 8.3(b)(iii) of these regulations shall be subject to a conformity reassessment procedure as Class III medical devices before the 1st March, 2004.

1.2.4. Decisions taken by notified bodies before the 1st September 2003 under regulation 8.3(a) of these regulations may not be extended.”.

Amends regulation
2 of the principal
regulations.

3. For regulation 2.1.3 and 2.1.3.1 of the principal regulations, there shall be substituted the following:

“2.1.3. Devices shall be divided into Classes I, IIa, IIb and III. Classification shall be carried out in accordance with Annex IX of the Directive, which is set out in Schedule IX to these regulations, read with Directive 2003/12.”.

Amends regulation
3 of the principal
regulations.

4. Immediately after regulation 3.1.21 of the principal regulations, there shall be inserted the following:

“3.1.22. “Directive 2003/12” means Commission Directive 2003/12/EC of 3rd February 2003 on the reclassification of breast implants in the framework of Directive 93/42/EEC concerning medical devices;

3.1.23. “animal” means an animal from a bovine, ovine or caprine species, as well as deer, elk, mink and cats;

3.1.24. “cell” means the smallest organised unit of any living form which is capable of independent existence and of replacement of its own substance in a suitable environment;

3.1.25. “derivative” means a material obtained from an animal tissue by a manufacturing process such as collagen, gelatine, monoclonal antibodies;

3.1.26. “Directive 2003/32” means Commission Directive 2003/32/EC of 23rd April 2003 introducing detailed specifications as regards the requirements laid down in Council Directive 93/42/EEC with respect to medical devices manufactured utilising tissues of animal origin;

3.1.27. “inactivation” means a process by which the ability to cause infection or pathogenic reaction by transmissible agents is reduced;

3.1.28. “non-viable” means having no potential for metabolism or multiplication;

3.1.29. “reduction, elimination or removal” means a process by which the number of transmissible agents is reduced, eliminated or removed in order to prevent infection or pathogenic reaction;

3.1.30. “source country” means the country in which the animal was born, has been reared and, or has been slaughtered;

3.1.31. “starting materials” means raw materials or any other product of animal origin out of which, or with the help of which, the devices referred to in regulation 2.2 of these regulations are produced;

3.1.32. “tissue” means an organisation of cells and/or extra-cellular constituents;

3.1.33. “transmissible agents” means unclassified pathogenic entities, prions and such entities as bovine spongiform encephalopathies agents and scrapie agents;

3.1.34. “TSE certificate” means TSE certificate of suitability issued by the European Directorate for the Quality of Medicines.”.

5. Regulations 4.6 and 4.7 of the principal regulations shall be renumbered as regulations 4.7 and 4.8 respectively and immediately after regulation 4.5.1 of the principal regulations, there shall be inserted the following:

Amends regulation 4 of the principal regulations.

“4.6. Subject to regulation 4.6.2 of these regulations, no person shall put into service or supply a relevant device (if that supply is also a placing on the market or if that supply is of a relevant device that has been placed on the market) if that device is manufactured utilising either animal tissue which is rendered non-viable or non-viable products derived from animal tissue unless—

(a) there is in respect of that device a risk analysis and risk management scheme which is in accordance with the requirements of Directive 2003/32; and

(b) the manufacturer of the device has fulfilled his obligations under the procedures within that scheme.

4.6.1. If collagen, gelatine or tallow is of animal origin and has been used in the manufacture of a relevant device, then subject to regulation 4.6.2 of these regulations, no person shall put into service or supply that device (if that supply is also a placing on the

market or if that supply is of a device that has been placed on the market), unless that collagen, gelatine or tallow was fit for human consumption.

4.6.2. Regulations 4.6 and 4.6.1 of these regulations shall not apply to a relevant device which is not intended to come into contact with the human body or which is intended to come into contact with intact skin only.”.

Amends regulation
5 of the principal
regulations.

6. Immediately after regulation 5.2 of the principal regulations, there shall be inserted the following:

“5.2.1. All necessary steps shall be taken to ensure that devices referred to in Article 1(1) of Directive 2003/32 are placed on the market and put into service only if they comply with the provisions of these regulations and the specifications laid down in Schedule XIII to these regulations.”.

Amends regulation
8 of the principal
regulations.

7. (1) Immediately after regulation 8.1 of the principal regulations, there shall be inserted the following:

“8.1.1. Before lodging an application for a conformity assessment pursuant to regulation 8.1 of these regulations, the manufacturer of medical devices referred to Article 1(1) of Directive 2003/32, shall carry out the risk analysis and the risk management scheme set out in Schedule XIII to these regulations.”.

(2) Immediately after regulation 8.12 of the principal regulations, there shall be added the following:

“8.13. Conformity assessment procedures for medical devices referred to in Article 1(1) of Directive 2003/32, shall include the evaluation of their compliance with the essential requirements of the Directive and the specifications laid down in the Annex to Directive 2003/32, which is set out in Schedule XIII to these regulations.

8.14. Notified bodies shall evaluate the manufacturer’s risk analysis and risk management strategy, and in particular:

(a) the information provided by the manufacturer;

(b) the justification for the use of animal tissues or derivatives;

(c) the results of elimination and, or inactivation studies or of literature search;

(d) the manufacturer's control of the sources of raw materials, finished products and subcontractors;

(e) the need to audit matters related to sourcing, including third party supplies.

8.15. Notified bodies shall, during the evaluation of the risk analysis and risk management in the framework of the conformity assessment procedure, take account of the TSE certificate, for starting materials, where available.

8.16. Except for medical devices using starting materials for which a TSE certificate has been issued as referred to in regulation 8.15, national bodies shall, through the CIGD, seek the opinion of the competent authorities of the other Member States on their evaluation of and conclusions on the risk analysis and risk management of the tissues or the derivatives intended to be incorporated in the medical device as established by the manufacturer.

8.16.1. Before issuing an EC design-examination certificate or an EC type-examination certificate, the notified bodies shall give due consideration to any comments received within 12 weeks from the date on which the opinion of the national competent authorities were sought.”.

8. Immediately after Schedule XII of the principal regulations, there shall be added the following Schedule:

Adds new Schedule XIII to the principal regulations.

“Schedule XIII

Based on the Annex of Directive 2003/32

1. RISK ANALYSIS AND RISK MANAGEMENT

1.1. Justification for the use of animal tissues or derivatives

The manufacturer must justify, on the basis of his overall risk analysis and risk management strategy for a specific medical device, the decision to use animal tissues or derivatives, referred to in Article 1(1) of Directive 2003/32, (specifying animal species and tissues) taking into account the expected clinical benefit, potential residual risk and suitable alternatives.

1.2. Assessment procedure

In order to ensure a high level of protection for patients or users, the manufacturer of devices utilising animal tissues or derivatives referred to in point 1.1 must implement an appropriate and well documented risk analysis and risk management strategy, to address all relevant relating aspects to TSE. He must identify the hazards associated with those tissues or derivatives, establish documentation on measures taken to minimise the risk of transmission and demonstrate the acceptability of the residual risk associated with the device utilising such tissues or derivatives, taking into account the intended use and the benefit of the device.

The safety of a device, in terms of its potential for passing on a transmissible agent, is dependent on all the factors described in points 1.2.1 to 1.2.7, which must be analysed, evaluated and managed. These measures in combination determine the device safety. There are two key steps that must be considered.

These are:

—selecting starting materials (tissues or derivatives) considered appropriate regarding their potential contamination with transmissible agents (see 1.2.1, 1.2.2 and 1.2.3) taking into account further processing,

—applying a production process to remove or inactivate transmissible agents on controlled sourced tissues or derivatives (see 1.2.4).

Furthermore, the characteristics of the device and its intended use must be taken into account (see 1.2.5, 1.2.6 and 1.2.7).

In performing the risk analysis and risk management strategy, due consideration must be given to opinions adopted by the relevant scientific committees, and where appropriate to the opinions of the Committee for Proprietary Medicinal Products CPMP, the references of which have been published in the Official Journal of the European Union.

1.2.1. *Animals as a source of material*

The TSE risk is related to the source species, strains and nature of the starting tissue. As the accumulation of TSE infectivity occurs over an incubation period of several years, sourcing from young healthy animals is considered to be a factor reducing the risk. Risk animals such as fallen stock, emergency slaughtered and TSE suspected animals must be excluded.

1.2.2. *Geographical sourcing*

Pending the classification of countries according to the BSE status in Regulation (EC) No 999/2001 of the European Parliament and of the Council of 22 May 2001 laying down rules for the prevention, control and eradication of certain transmissible spongiform encephalopathies¹², the Geographical BSE risk (GBR) is used when assessing the risk of the source country. The GBR is a qualitative indicator of the likelihood of the presence of one or more cattle being infected with BSE, pre-clinically as well as clinically, at a given point in time, in a country. Where presence is confirmed, the GBR gives an indication of the level of infection as specified in the table below.

GBR level	Presence of one or more cattle clinically or pre-clinically infected with the BSE agent in a geographical region/country
I	Highly unlikely
II	Unlikely but not excluded
III	Likely but not confirmed or confirmed, at a lower level
IV	Confirmed, at a higher level

Certain factors influence the geographical risk of BSE infection associated with the use of raw tissues or derivatives from individual countries. These factors are defined in Article 2.3.13.2, point 1) of the International Animal Health Code of the OIE (Office International des Épidémiologies), which is available at web-site www.oie.int/eng/normes/Mcode/A_00067.htm

The Scientific Steering Committee has made an assessment of Geographical BSE Risk (GBR) of several third countries and Member States, and will continue to do so for all the countries, which applied for BSE status categorisation, taking the main OIE factors into account.

1.2.3. *Nature of starting tissue*

The manufacturer must take into account the classification of the hazards relating to different type of starting tissue. Sourcing of animal tissue must be subject to control and individual inspection by a veterinarian and the animal carcass must be certified as fit for human consumption.

¹² OJ No. L 147, 31-05-2001, P.1.

The manufacturer must ensure that no risk of cross-contamination occurs at the time of slaughtering.

The manufacturer must not source animal tissue or derivatives classified as potentially high TSE infectivity, unless sourcing of these materials is necessary in exceptional circumstances, taking into account the important benefit for the patient and the absence of an alternative starting tissue.

In addition, the provisions in Regulation (EC) No 1774/2002 of the European Parliament and of the Council of 3 October 2002 laying down health rules concerning animal by-products not intended for human consumption must be applied.

1.2.3.1. Sheep and goats

A classification of infectivity in tissues for sheep and goats has been established based on actual knowledge on the basis of the titres of transmissible agents in tissues and body fluids from naturally infected sheep and goats with clinical scrapie. A table was presented in the Scientific Steering Committee (SSC) opinion of 22-23 July 1999 on 'The policy of breeding and genotyping of sheep', (as an annex)¹³ and further updated in the opinion of the SSC — TSE infectivity distributed in ruminant tissues state of knowledge December 2001 — adopted 10-11 January 2002¹⁴.

The classification may be reviewed in the light of new scientific evidence (for example using relevant opinions from the Scientific Committees, the Committee for Proprietary Medicinal Products CPMP and Commission Measures regulating the use of material presenting risks as regards TSE). A review of the references to relevant documents/opinions will be published in the Official Journal of the European Union and will be listed after a Commission Decision has been taken.

1.2.3.2. Cattle

The list of specified risk material (SRM) laid down in Regulation (EC) No 999/2001 shall be considered as potentially high TSE infective.

1.2.4. *Inactivation or removal of transmissible agents*

1.2.4.1. For devices which cannot withstand an inactivation/elimination process without undergoing unacceptable degradation, the manufacturer must rely principally on the control of sourcing.

1.2.4.2. For other devices, if claims are made by the manufacturer for the ability of manufacturing processes to remove or inactivate transmissible agents, these will have to be substantiated by appropriate documentation.

¹³ Available on the website of the Commission
http://europa.eu.int/comm/food/fs/sc/ssc/outcome_en.html.

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Relevant information from an appropriate scientific literature search and analysis can be used to support inactivation/elimination factors, where the specific processes referred to the literature are comparable to those used for the device. This search and analysis should also cover the available scientific opinions that may have been adopted by a EU Scientific Committee. These opinions shall serve as a reference, in cases where there are conflicting opinions.

When the literature search failed to substantiate the claims, the manufacturer must set up a specific inactivation and/or elimination study on a scientific basis and the following need to be considered:

- the identified hazard associated with the tissue,
- identification of the relevant model agents,
- rationale for the choice of the particular combinations of model agents,
- identification of stage chosen to eliminate and/or inactivate the transmissible agents,
- calculation of the reduction factors.

A final report must identify manufacturing parameters and limits that are critical to the effectiveness of the inactivation or elimination process.

Appropriate documented procedures must be applied to ensure that the validated processing parameters are applied during routine manufacture.

1.2.5. Quantities of animal starting tissues or derivatives required to produce one unit of the medical device

The manufacturer must evaluate the quantity of raw tissues or derivatives of animal origin required to produce a single unit of the medical device. Where a purification process is involved, the manufacturer must assess whether it may have the potential to concentrate levels of transmissible agents present in the animal starting tissues or derivatives.

1.2.6. Tissues or derivatives of animal origin coming into contact with the patients and users

The manufacturer must consider:

- (i) the quantity of animal tissues or derivatives;
- (ii) the contact area: its surface, type (e.g. skin, mucous tissue, brain) and condition (e.g. healthy or damaged);

(iii) the type of the tissues or derivatives coming into contact with the patients and/or users; and

(iv) how long the device is intended to remain in contact with the body (including bioresorption effect).

The number of medical devices that could be used in a given procedure shall be taken into account.

1.2.7. Route of administration

The manufacturer must take into account the route of administration recommended in the product information, from the highest risk down to the lowest.

1.3. Review of the assessment

The manufacturer must establish and maintain a systematic procedure to review information gained about their medical device or similar devices in the post-production phase. The information must be evaluated for possible relevance to safety, especially:

- (a) if previously unrecognised hazards are detected;
- (b) if the estimated risk arising from a hazard is no longer acceptable;
- (c) if the original assessment is otherwise invalidated.

If any of the above apply, the results of the evaluation shall be fed back as an input to the risk management process.

In the light of this new information, a review of the appropriate risk management measures for the device must be considered (including rationale for choosing an animal tissue or derivative). If there is a potential that the residual risk or its acceptability has changed, the impact on previously implemented risk control measures must be re-evaluated and justified.

The results of this evaluation must be documented.

2. EVALUATION OF CLASS III MEDICAL DEVICES BY NOTIFIED BODIES

For devices falling into Class III under rule 17¹⁵ of Annex IX to the Directive, set out in Schedule IX to these regulations, manufacturers must provide to the notified bodies referred to in Article 4 of Directive 2003/32, all relevant information to allow evaluation of their current risk analysis and risk management strategy.

¹⁵ All medical devices utilising animal tissues or derivatives rendered non-viable except devices intended to come into contact with intact skin only.

Any new information on TSE risk, collected by the manufacturer and relevant for their devices must be sent to the notified body for information.

Any change in relation to processes of sourcing, collection, handling and inactivation/elimination and that could modify the result of the manufacturer's risk management dossier must be transmitted to the notified body for the purpose of an additional approval prior to its implementation.”.