Superior Health Council

RECOMMENDATIONS OF THE SUPERIOR HEALTH COUNCIL no. 9162

Recommendations concerning the community quality standards for medical devices manufactured utilising tissues of animal origin and intended for use in human beings.

The Superior Health Council has issued guidelines to ensure the quality and safety of implants of animal origin from the production unit to their implantation in humans.

December 2014

1. INTRODUCTION

Public health protection, food chain safety, animal health and animal welfare are legally regulated as a consequence of the rules on materials of animal origin used in farming (primary products of animal origin found in the food chain and animal by-products not intended for human consumption) and for scientific research (laboratory animals). Animal by-products can be processed as a constituent in animal feeds, for example, or used in the production of medicines, cosmetics, leather, fertilisers, etc.

All medical devices that are intended for use in human beings are covered by legislation at the European level. Belgium has several federal and regional laws covering the legislative aspects, but only in a fragmentary way. These aspects are covered in detail in point 3.3. (Regulatory Framework). This situation has led the group to establish a set of rules of good practice covering the microbiological quality of the materials of animal origin used to develop, manufacture and provide implants of animal origin and invasive devices intended for use in human beings (see Appendix 1. Definitions).

The recommendations are all the more important given that these products are already on the market and help bring about improvements in public health. There are surgical haemostatic agents, for example, based on materials of animal origin made from collagen, gelatine and/or thrombin from porcine and/or bovine species. In surgery, neurosurgeons are now able to replace parts of the dura mater with a synthetic product or tissue of animal origin. Ligaments from the horse, collagen from the foetal skin tissue of the cow and intestinal submucosa from the pig are currently available on the market. These products are relatively more expensive than their synthetic alternatives, but in some situations their application can be considered more appropriate, such as for a hernia repair in a contaminated/infected surgical field (Breuing et al., 2010).

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Given that these recommendations identify the potential risk and propose good production practices for implants of animal origin (from production unit to application of the end product), they can serve as a basic reference point for research, industry (biotechnology, etc.) and any other partner in the realm of healthcare. The Commission for the reimbursement of implants and invasive medical devices has a particular interest in this, in view of the information needed to complete the reimbursement application form.

2. RECOMMENDATIONS

Responsibility for the quality of the product lies with the manufacturer. To ensure this quality, the Superior Health Council (SHC) recommends that particular attention be given to the following four points:

- state of health of the source animals;
- traceability of data throughout the chain, from production to processing and distribution of invasive devices and implants of animal origin intended for use in human beings;
- a risk assessment of pathogenic agents;
- minimisation of the risks, through implementation of suitable protocols.

In addition, all players involved must work together to ensure vigilance.

Finally, the SHC advocates the set-up of an automated and centralised system of product traceability. A system of this type permits anticipation for any choice of containment prompted by the discovery of a reaction/event related to contamination of an implant of animal origin.

Keywords

Keywords	**MeSH terms***	**Sleutelwoorden**	**Mots clés**	**Schlüsselwörter**
Medical device	Equipment and supplies	Medische hulpmiddel	Dispositif médical	Medizinprodukt
Invasive medical device	Equipment and Supplies / Surgical Procedures, Operative	Invasief medische hulpmiddel	Dispositif médical invasif	Invasives Medizinprodukt
Implant of animal origin	Prostheses and Implants / Animals	Implantaat van dierlijke oorsprong	Implant d'origine animale	Implantat tierischen Ursprungs
Porcine species	Porcine	Varkens	Espèce porcine	Schweine
Equine species	Equidae	Paarden	Espèce équine	Pferde
Bovine species	Cattle	Runderen	Espèce bovine	Rinder
Risk assessment	Risk assessment	Risicobeoordeling	Evaluation du risque	Risikobewertung
Human application	Cell- and Tissue-Based Therapy / Humans	Menselijk toepassing	Application humaine	Anwendung beim Menschen
Pathogenic agent	Host-Pathogen Interactions	Pathogeen agens	Agent pathogène	Krankheitserreger

** MeSH (Medical Subject Headings) is the NLM controlled vocabulary thesaurus used for indexing articles for PubMed.*

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3. OBJECTIVES AND RATIONALE

List of abbreviations

BSE	Bovine spongiform encephalopathy
CMM	Committee on Medical Materials
EMA	European Medicines Agency
SAR	Serious adverse reaction
SAE	Serious adverse event
EUnetHTA	European network for health technology assessment (the scientific and technical cooperation of the HTA Network)
EU	European Union
FAMHP	Federal Agency for Medicines and Health Products
SHC	Superior Health Council
HTC	Human tissues and cells
MRSA	Methicillin-resistant Staphylococcus Aureus
OECD	Organisation for Economic Co-operation and Development
TSE	Transmissible spongiform encephalopathies
SPF	Specific pathogen free
SOP	Standard operating protocol
vCJD	Variant Creutzfeldt-Jakob disease
OIE	World Organisation for Animal Health
WHO	World Health Organisation

3.1. Methodology

Having assessed the application, the Board and the chairman of the study group identified the expertise needed. The group experts submitted a general declaration of interests and an ad-hoc statement. The potential for a conflict of interests was assessed by the Committee for Deontology and Ethics.

The recommendations are based on a reading of the scientific literature (international magazines with reading committees), the reports and standards of international authorities, the opinion of the experts and any other relevant information.

Once the draft recommendations were approved by the ad-hoc working group, made up of representatives from the permanent “Cells, tissues and organs of human and animal origin” study group, and a panel of experts on contagious animal diseases, the recommendations were discussed with a representative of the Federal Agency for Medicines and Health Products (FAMHP) and presented to the members of the permanent study group. The Board of the SHC was the final authority to validate the recommendations.

3.2. Limitations/framework/scope of the recommendations

The term xenotransplantation refers to the transplantation of cells, tissues and organs of animal origin. In broad terms, xenotransplantation is any procedure or operation by which cells, tissues or organs of animal origin are transplanted, implanted or administered to a human recipient by means of perfusion. This definition covers the transplantation of non-living biomaterial or acellular material (Appendix 1 - Definition) (e.g. heart valves, blood vessels, ligaments, collagen) as well

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as living biomaterial (e.g. hepatic cells or pancreatic cells) from animal species. The non-living biomaterial or acellular material carries an appreciably smaller risk when it comes to the transmission of (infectious) diseases. The transplantation of cells and/or organs of animal origin, which is still in an experimental stage, is designed to save human lives (e.g. liver transplants), whereas this is seldom the case, for medical devices and implants of animal origin, a few exceptions aside, such as heart valves.

When it comes to the xenotransplantation of living biomaterial, practitioners have gained the majority of their experience in non-human primates (baboons, etc.) and pigs. However, this document does not cover the xenotransplantation of organs, tissues and cells originating from primates because the procedure is not carried out in Belgium at the present time. To compensate for the lack of information on non-living biomaterial, these recommendations refer in places to the literature specific to the transplantation of living biomaterial.

These recommendations are confined to non-living materials of animal origin. Pharmaceuticals composed of or containing materials of animal origin are beyond the scope of the present recommendations. Both are entangled in a specific framework (EUNETHTA, 2013). The present recommendations do not take any of the Advanced therapy medicinal products (ATMP) regulations into account.

At the present time, the following animal species are used in the manufacture of invasive medical devices and implants: porcine, bovine and equine. Largely for this reason and due to the scarcity of literature on the subject (aside from the paragraph on transmissible spongiform encephalopathies (TSE)), the recommendations are confined to implants originating from these three species.

The recommendations are specific to the risk of transmitting viral, bacterial, parasitic and fungal infection, as well as TSE. Currently, surgeons may, but not necessarily, have access to information on the products available on the market, such as: information on sterilisation or the statement *"this product does not present a risk of contracting a prion disease"*. All materials of animal origin intended for use in human beings must be sterile.

The recommendations relate to the procurement, harvesting, testing, processing, storage and distribution of invasive medical devices and implants of animal origin intended for use in human beings. They take account of the national legislation and the prevailing European and international requirements and recommendations (EMA, 2011). These recommendations do not cover biocompatibility tests (cytotoxicity, immunotoxicity, systemic toxicity, genotoxicity, etc.).

Animal welfare concerns in the biomedical sector and ethical problems associated with xenotransplantation are beyond the scope of the present recommendations, but should be assessed by the competent authority in an ensuing stage.

Problems similar to those discussed in the present recommendations occur in implants of animal origin other than those described here (porcine, bovine, equine) and in other therapeutic products. The rationale of the present document may offer food for thought for these products.

Superior Health Council
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3.3. Legislative framework

The legal basis is provided by Regulation (EC) No. 1069/2009 of 21 October 2009[1] and its accompanying implementing Regulation (European Union (EU)) no. 142/2011. More particularly, they indicate:

- a risk-based classification of animal by-products (category 1 - 3 materials), which indicates whether they can be used in animal feed, in the manufacture of technical products or products for other purposes, or must be destroyed;
- an obligation on the part of Member States and operators to collect and dispose of animal by-products as quickly as possible;
- the exclusion of products which are not suitable for human consumption from the breeding stock food chain; and
- finally, a ban on feeding an animal species with material originating from the same species ("prohibited re-use within the same species").

Animal by-products from every category of materials can be used in the manufacture of derived products such as active implantable medical devices, medical devices, medical devices for in-vitro diagnostics and medicines.
Lists of establishments registered and accredited in Belgium and the EU pursuant to Regulation (EC) No 1069/2009 are available.

The international standard - EN-ISO 13485:2012 *Quality Management System* - specifies requirements for a quality management system for implementation in an organisation that designs, develops, produces, installs and maintains medical devices and designs, develops and provides related services. These recommendations do not cover ISO standard 13485.

These recommendations must be read in the context of Regulation **(EU) No 722/2012** concerning particular requirements with respect to medical devices manufactured utilising tissues of animal origin.

3.4. Development of the recommendations

The recommendations refer to the available literature and, where no specific literature can be found, to the more strict literature available in related areas such as xenotransplantation and human tissues and cells (HTC), where other risks come into play.

The recommendations are organised in the following manner:

1. Elements that identify the hazards;
2. Elements that characterise the hazards;
3. General measures to limit the risk;
4. Specific measures to limit the risk.

[1] EU – European Union. Regulation (EC) No 1069/2009 of the European Parliament and of the Council of 21 October 2009 laying down health rules as regards animal by-products and derived products not intended for human consumption and repealing Regulation (EC) No 1774/2002 (Animal by-products Regulation); 2009.

3.4.1. Elements that identify the hazards

Elements to identify the hazards were determined, assessed and gathered from the existing literature. However, the literature does not provide all the information needed. The information on porcine species is easiest to access because this material is frequently used as a resource in xenotransplantation and research. Unfortunately, the same cannot be said for bovine species, nor equine species for that matter. These discrepancies in the information explain the incongruity of the relevant paragraphs.

We can identify two types of hazards:

- non-specific infections and infestations originating from non- or mildly pathogenic commensal microbiota in the original animal species;
- specific infections by well identified pathogenic (micro)organisms that may have zoonotic potential.

The recommendations are confined to these two categories.

3.4.1.1. Infectious agents

In the chapter entitled “infectious agents” it is essential to take into account:

- the epidemiological situation in what may be a very distant country, where the material was harvested and/or the region from which the implants originate;
- the unknown status of the recipient, who may belong to a higher risk subpopulation (such as immunocompromised patients).

More than 1,415 pathogenic agents cause infectious diseases in human beings, 616 in livestock and 374 in carnivorous pets (Cleaveland et al., 2001).

A. Viruses

Generally speaking, the viruses present the greatest risk for establishment and dissemination through transplantation. Since the group is not homogenous, the risks must be considered separately. Some viruses pose a real threat, whereas in others, the threat is negligible. The transmission of persistent chronic or latent viruses capable of affecting a large number of people could have a significant effect on public health.

The problems caused by known zoonotic viruses may not differ from those caused by other viruses transmitted by classic means. However, these viruses could generate a high risk to individual recipients from an increased risk subpopulation .

Animal viruses that are not known to be zoonotic may possibly constitute a risk because they could acquire a tropism towards human beings through genetic evolution. In this context, viruses with a high level of mutation could pose a high risk (e.g. influenza virus, rotavirus, coronavirus, etc.).

Unknown agents present an inherent problem (WHO, 1998). For the added guarantee of being able to inactivate viruses that are not known at the present time, the procedures should be capable of inactivating the most resistant viruses.

B. Bacteria

The document "*Xenotransplantation: Guidance on infectious disease prevention and management*" (WHO, 1998) states that the risk generated by bacteria to the general population is probably no greater than in (human) allotransplantation. The effects of exposure to bacteria are more a function of the recipient's immune status than the pathogenic potential of the bacteria. We therefore refer specifically to the relevant legislation and to the recommendations on allotransplantations of human origin (Law, 2008; RD, 2009; SHC 8716, 2013; SHC 8143, 2008; SHC 8785, 2012; SHC 8763, 2014).

C. Parasites

Helminths, protozoa and rickettsia with zoonotic properties may present a risk of infection. Animal parasitic agents that are not known as zoonotic pathogens may also constitute a risk. The exact level of risk depends largely on the type of tissue or material harvested. This is because most parasites have a specific tissue tropism and specific life cycle requirements. The presence of certain parasites will depend on the climate and environment in the country or region from which the animal comes or through which it is transported. The origin of the harvested tissue or material will therefore also affect the level of the risk.

Particular care must be taken in respect of possible parasitic infection of the animal source material during harvesting and processing.

However, the effects must also be related to the recipient's immune status, in much the same way that they are reported for some haemoparasites of the *Babesia* species (Lempereur et al., 2015).

D. *Fungi and yeasts*

The document "*Xenotransplantation: Guidance on infectious disease prevention and management*" (WHO, 1998) states that the risk posed by fungi and yeasts to the general population is probably no greater than in (human) allotransplantation. The effects are more a function of the recipient's immune status than of the agents themselves. We therefore refer specifically to the relevant legislation and to the recommendations on allotransplantations of human origin (Law, 2008; RD, 2009; SHC 8716, 2013; SHC 8143, 2008; SHC 8785, 2012; SHC 8763, 2014).

E. Prions - TSE agents

The TSE agents of particular interest are those found in ruminants, i.e. bovine spongiform encephalopathy (BSE) in cattle and scrapies in sheep and goats. The iatrogenic transmission of TSE agents has already been demonstrated. There are documented cases of variant Creutzfeldt-Jakob disease (vCJD) caused by the transmission of BSE agents to humans.

3.4.1.2. Animal species: **bovine**

A recent review has yielded a non-exclusive list (McDaniel et al., 2014).

Bacteria are the main taxonomic group of pathogenic (micro)organisms of bovine origin transmissible to humans either by (in)direct infection (inhalation, ingestion, absorption through the skin, etc.) or through foods or biological vectors (McDaniel et al., 2014). They are followed by parasites, viruses, fungi and yeast and prions. In epidemiological terms, bacterial zoonoses are largely spread around the world, aside from those that are transmitted via biological vectors. Though most of these pathogens have been eradicated in much of Europe, they continue to exist in other regions of the world[2] and thus constitute a real threat in the context of implants of animal origin. A short list of bovine pathogens with zoonotic potential can be found in the same publication (McDaniel et al., 2014), along with their (re)appearance status. The most important are given in alphabetical order below:

- **Viruses**: Cowpox virus, Crimean-Congo haemorrhagic fever virus, Ecthyma contagiosa virus, Kyasanur Forest disease virus, Pseudocowpox virus, Rabies virus, Rift Valley fever virus, Tick-borne encephalitis virus.

- **Bacteria**: *Bacillus anthracis* (anthrax), *Brucella* spp., *Burkholderia pseudomallei*, *Campylobacter jejuni*, *Clostridum difficile*, *Coxiella burnetii* (Q fever), *Escherichia coli, Leptospira* spp., *Listeria monocytogenes*, *Mycobacterium* spp., *Salmonella* spp., *Staphylococcus aureus*.

- **Parasites**: *Anaplasma phagocytophilum*, *Ascaris suum, Babesia* spp., *Cryptosporidium* spp., *Dracunculus medinensis, Dicrocoelium dentriticum, Dicrocoelium hospes, Echinococcus granulosus, Entamoeba histolytica*, *Fasciola* spp., *Giardia intestinalis, Gongylonema pulchrum, Mammomonogamus* spp., *Rickettsia conorii, Rickettsia africae, Sarcocystis bovihominis, Schistosoma* spp., *Taenia saginata, Toxoplasma gondii, Trichinella spiralis, Trichostrongylus* spp., *Trypanosoma brucei gambiense, Trypanosoma brucei rhodesiense.*

- **Fungi**: *Aspergillus* spp., *Coccidioides immitis, Histoplasma capsulatum, Microsporum* spp., *Sporothrix schenckii, Trichophyton* spp.

- **Non-conventional transmissible agents/TSE**: BSE agents

The treatment options and risk of mortality (e.g. high mortality: *Rift Valley fever*, *Crimean-Congo haemorrhagic fever*, *Q fever* and anthrax) are highly varied in these cases (McDaniel et al., 2014).

3.4.1.3. Animal species: equine

Viruses are the main taxonomic group of pathogenic (micro)organisms of equine origin transmissible to humans either by (in)direct infection (inhalation, ingestion, absorption through the skin, etc.) or through foods or biological vectors (Chomel et al., 2003). They are followed by bacteria, parasites and fungi and yeast. As is the case with cattle, several of these pathogens

[2] Information on the situation with regard to animal diseases can be found on the world animal health information database interface, WAHID, which is available at the following URL address: http://www.oie.int/wahis_2/public/wahid.php/Wahidhome/Home/indexcontent/newlang

have been eradicated in much of Europe, but continue to exist in other regions of the world[3] and thus constitute a real threat in the context of implants of animal origin.

Below is a short list in alphabetical order of the main pathogens with zoonotic potential among horses (Chomel et al., 2003):

- **Viruses**: Borna virus, Eastern equine encephalitis virus, Hendra virus, Japanese encephalitis virus, Rabies virus, Venezuelan equine encephalitis virus, Vesicular stomatitis virus, Western equine encephalitis virus, West-Nile fever virus.

- **Bacteria**: *Bacillus anthracis*, *Burkholderai mallei, Burkholderia pseudomallei*, *Dermatophilus congolensis*, *Leptospira* spp., *Rhodococcus equi*, *Salmonella* spp., *Streptococcus equi* subsp. *Zooepidemicus*.

  Parasites: *Anaplasma phagocytophilum*, *Cryptosporidium* spp., *Dracunculus medinensis Dricocoelium dentriticum, Echinococcus granulosus, Echinococcus multilocularis, Fasciola* spp., *Giardia intestinalis, Gongylonema pulchrum, Rhinosporidium seeberi, Schistosoma* spp., *Toxoplasma gondii, Trichinella spiralis.*

- **Fungi**: *Aspergillus* spp., *Blastomyces dermatitidis, Histoplasma capsulatum, Trichophyton* spp.

- **Non-conventional transmissible agents/TSE**: Not applicable

3.4.1.4. Animal species - porcine

Viruses are the main taxonomic group of pathogenic (micro)organisms of porcine origin transmissible to humans either by (in)direct infection (inhalation, ingestion, absorption through the skin, etc.) or through foods or biological vectors (Smith et al., 2011). They are followed by bacteria, parasites and fungi and yeast. As is the case with cattle and horses, several of these pathogens have been eradicated in much of Europe, but continue to exist in other regions of the world[4] and thus constitute a real threat in the context of implants of animal origin.

The abridged list below gives in alphabetical order the main pathogens with zoonotic potential among pigs according to their appearance/reappearance status (Smith et al., 2011):

- **Viruses**: Hepatitis E virus, Influenza virus, Japanese encephalitis virus, Vesicular stomatitis virus.

- **Bacteria**: *Bordetella bronchiseptica, Clostridium difficile*, *Erysipelothrix rhusiopathiae, Leptospira* spp., *Mycobacterium* spp., *Rhodococcus equi, Salmonella* spp., *Staphylococcus aureus* (including methicillin resistant strains, MRSA), *Streptococcus suis* (Levett, 2001, Reboli & Farrar, 1898, *Woolfrey & Moody, 1991*).

[3] Information on the situation with regard to animal diseases can be found on the world animal health information database interface, WAHID, which is available at the following URL address:
http://www.oie.int/wahis_2/public/wahid.php/Wahidhome/Home/indexcontent/newlang

[4] Information on the situation with regard to animal diseases can be found on the world animal health information database interface, WAHID, which is available at the following URL address:
http://www.oie.int/wahis_2/public/wahid.php/Wahidhome/Home/indexcontent/newlang

Parasites: *Ascaris suum, Balantidium coli, Clonorchis sinensis, Cryptosporidium* spp*., Dicrocoelium dentriticum, Dicrocoelium hospes, Diphyllobothrium latum, Echinococcus granulosus, Echinococcus multilocularis, Entamoeba histolytica, Fasciola* spp*., Fasciolopsis buski, Gastrodiscoides hominis, Giardia intestinalis, Gongylonema pulchrum, Opisthorchis felineus, Paragonimus westermani, Sarcocystis suihominis, Schistosoma* spp*., Taenia solium, Toxoplasma gondii, Trichinella spiralis, Trichuris suis.*

- **Fungi**: **-**

- **Non-conventional transmissible agents/TSE**: nonatural case or specific TSE agent has been established in pigs. However, tests have shown that pigs are susceptible to the BSE agent.

3.4.2. Elements that characterise the hazards

Though information is available on the properties of potentially infectious pathogenic agents, scientific publications rarely provide proof of transmission sufficient to allow us to document the potential risk in the context of these recommendations.

Known infectious zoonotic agents in animals can cause disease in human beings, as can mildly or non-pathogenic (micro)organisms in a number of microbiota among immunocompromised patients. Pathogenic agents that can infect both humans and animals are increasingly recognised as a major source of emerging conditions among human beings (Jones et al., 2008).

The recommendations must also take account of the fact that the recipient is not specified, as in the case of invasive medical devices, and that the situation could be different when the recipient would be immunocompromised, for example. The products must be applicable, without risk, to all recipient population groups.

3.4.3. General measures to limit the risk of infection

Since it would be impossible to avoid the use of material of animal origin in the production of some products, thereby entirely eliminating the risk of infectious disease transmission, the risk must be kept to a minimum. An adequate safety and monitoring programme would involve the principle of prevention and the introduction of adequate tracing procedures and tests for the source animals. This prevention principle implies that although the risk of transmitting infection through invasive devices and implants of animal origin is generally acknowledged as low, there is no reason to wait for confirmation of the risk before taking the necessary corrective measures (OECD/WHO, 2011).

3.4.3.1. General organisation and quality

A responsible person must be appointed having qualifications and responsibilities (manufacturer) of the animal tissues and cells , who must have at least two years of practical experience in the management of animal tissues and cells, including quality, safety and traceability. The authorities

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and responsibilities of the animal tissues and cells responsible person are on a par with those of the human tissues and cells responsible person. They are set out in Appendix 2 of the present recommendations.

In accordance with RD 1/09/2011, a manufacturer is defined as: “a natural or legal person who is responsible for the design, manufacture, packaging and labelling of a device with a view to bringing it to market in his, her or its own name, no matter whether these actions are carried out by the same person or on his, her or its account by a third party” and a person suited to the role of responsible person.

3.4.3.2. Procurement and harvesting

Point 8.2. of Appendix 1 of the RD of 18/03/1999 (amended on 01/09/2011) makes reference in the second paragraph to procurement and harvesting: “Tissues of animal origin must originate from animals that have been subject to veterinary inspections and controls appropriate for the intended use of the tissues. The stated authorities record information on the geographical origin of the animals. The processing, storage, testing and handling of tissue, cells and substances of animal origin must be such that optimal safety is ensured. More particularly, safety with regard to viruses and other transmissible agents must be guaranteed through the application of validated methods designed to eliminate or inactivate viruses in the course of the production process. This is an essential element in ensuring the safety of these products”.

The organisation responsible for the processing of the raw material and the distribution of the end product must have a protocol related to the practical organisation of screening and harvesting. If screening and harvesting of the source material is entrusted to a third party, there must be a written contract between the responsible organisation and this third party. It must specify things such as the type of source material to be procured and the protocols to be followed. These third parties must have the relevant qualifications, a suitable organisation and teams of people with the competences needed to procure and harvest the source material.

The source animal selection criteria must rely on an analysis of the risks relative to the use of that particular source material. These criteria must be documented.

It is advisable to avoid the risk factors so as to lower the risk of infectious disease transmission. The need to minimise the transmission risk affects the choice of animal species. Other important factors are availability and animal welfare. At the present time, the animal origin of implants and invasive medical devices intended for use in human beings is largely restricted to bovine, equine and porcine species.

Before selecting a particular animal species as a source of material, public health aspects need to be taken into consideration .

The raw material may only be obtained from breeding stock originating from registered facilities at which systematic documentation is kept on the origin of the animals (certificate, country, species, etc.) and their previous health history. The animals must be slaughtered in a suitable environment prior to harvesting of the material. The rules of hygiene and sterility must be followed strictly in order to keep the risk of contamination, chiefly through faecal material, to a minimum. Appropriate basic measures must be taken with regard to the source animals to prevent infection and the dissemination of

infectious agents. In particular, measures must be put in place to ensure biosafety at the facility of origin (Saegerman et al., 2012). A supervision programme must be set up. The source animals must be housed in suitable units. Critical phases of the source animals' rearing and growth must be described in standard operating protocols (FDA, 2001).

The precautions taken to reduce the risk of infection must be put in place in all stages of production and must be conformant with the predefined protocols.

To minimise the risk of zoonoses it is advisable that the following donors be used in descending order of importance:

- a germ-free animal, meaning free of all microorganisms.
- a gnotobiotic animal is by definition (see Appendix 1) germ-free at birth and is then infected with known microorganisms in an experimental context.
- A specific pathogen free (SPF) animal is an animal that is free of certain, specific microorganisms. The list of specific pathogens must be compared against the list of microorganisms in the present recommendations (hazard analysis). In the case of non-SPF organisms, additional information must be provided on the potential risk. Once the producer is able to demonstrate that the donor animals are free of all potential zoonotic microorganisms, the animals no longer need to be considered as a source of infection.
- "Conventional" animals for which the specific microbial status is unknown or is not adequately known must not be used to produce materials of animal origin intended for use in human beings. If infected, even at some time in the past, a potential source animal must be rejected.

It has already been proven that iatrogenic transmission of TSE agents is possible. It has also been demonstrated that variant Creutzfeldt-Jakob disease (vCJD) is caused by transmission of the BSE agent to humans. We therefore recommend that materials from animal species which are naturally susceptible to TSE agents not be used (for example: *Bioglue® ; cattle exclusively from BSE-free countries)*.

The harvesting period must be as brief as possible. The person or persons whose job it is to harvest the raw material must have knowledge of and experience with the properties specific to the harvested material. The standard operating protocols (SOPs) for harvesting the raw material must ensure that the properties of the raw material remain suited to its eventual use and that the risks of microbiological contamination and transmissible disease are kept to a minimum. To this end, harvesting must take place in suitable rooms in accordance with procedures designed to minimise the risk of microbial and other types of contamination of the harvested animal tissues and cells and in accordance with practical regulations that would apply to any surgical intervention. The instruments and equipment must be disposable or it must be possible to sterilise them in an appropriate manner. Special circumstances or incidents that occur during harvesting and which could affect the quality of the material harvested must be reported and analysed by the head of the organisation that handles processing and distribution. A harvest file (identification of the source animal, identification and signature of the person charged with obtaining the material, date, place) must be created for each source animal and given to the addressee of the source material. This information must be kept in a register. Once harvested, the raw material must be packaged in such a way as to minimise the risk of contamination for the harvested material and any person who transports it and to create the conditions (temperature, etc.) needed to ensure proper storage of the raw material. The type of transport must be chosen in accordance with the

general transport regulations and a validated procedure that satisfies the safety and storage criteria for every type of raw material. The harvested material and accompanying documentation must be identified and verified on receipt.

Preventive measures put in place in relation to final screening, qualification of the source animals and harvesting of the source material must be sufficient to minimise the risk of infectious agent transmission. In principle, source animals must be kept in quarantine for three weeks prior to the harvest of the source material. During this period, the animals will be given veterinary examinations and screened for infectious agents using appropriate tests, including serological and microbiological analyses. These tests will be carried out on relevant biological samples according to the pathogen, species and epidemiological situation in the region of origin. Serological testing involves medical devices for in-vitro diagnostic examination carrying the CE label or documenting appropriate validation. These tests must be carried out in an appropriately accredited laboratory.

3.4.3.3. Processing, preservation and storage

All stages of processing (including organ culture and cell culture, decontamination, etc.) will take place in predetermined conditions designed to guarantee the quality of the products and the safety of the personnel. The methods of preparation must describe the actual processing procedures, the equipment needed, the preparation media, additional therapeutic products and the tests to be carried out. The rules concerning personnel, rooms and equipment have been explained in the paragraphs above, as have those concerning quality control, testing and documentation. If any step of the process is outsourced, it must be covered by a separate agreement. The critical processing procedures must be identified and validated. They must not render the product clinically ineffective or hazardous to the recipient. Once the processing procedures for every product type are validated, they must be described in SOPs that specify the chronology of the steps to be taken and satisfy the safety and processing criteria particular to every tissue and cell type. These procedures and conditions are described in greater detail in specific quality standards.

Examples:

- use of solvents to extract fats and lipids;
- use of trypsin to remove every living cell and non-collagen waste;
- glycerol treatment;
- lyophilisation;
- etc.

When specific media are brought in contact with the product during processing or therapeutic products are added, the choice of said media and products, their properties, origin and testing, as well as the asepsis and labelling rules must be described in SOPs. When using processing media and/or additional therapeutic products, the origin, batch number and expiry date must be stated in the documentation for the relevant processing steps.
To prevent cross-contamination, material from one source animal must not at any time during harvesting, preparation or storage come into contact with material from another animal.

All preservation and storage steps must take place under predetermined conditions designed to guarantee the quality of the end product and the safety of the personnel. This means that the

SOPs for the preservation procedures must specify the temperature limits within which the end product is to be stored. They must also state the time limits within which they are to be kept at a given temperature (if several storage temperatures are possible).

3.4.4. Specific measures to reduce the risk of infection

The following measures were inspired by medical practice in relation to HTC (Law of 19/12/2008, RD 2008). The fact that they are acceptable for HTC means that they can be "extrapolated" to animal material.

3.4.4.1. Minimum requirements for microbiological testing - checks and inactivation

There must be appropriate screening for known infectious agents in the herd, the individual source animal and the source material. Tests in relation to serological and immunological screening must be based on specific infectious agents associated with the source animal type, its zoonotic character, the origin of the animal and the intended use in human beings. The tests (molecular biological tests included) must be selected on the basis of their characteristics (sensitivity, specificity, repeatability and reproducibility). Tests of the individual source animal must be carried out no more than 3 months prior to the harvesting of the source material. All products intended for transplantation must be microbiologically tested using bacteria, fungi and yeast and wherever necessary mycoplasma (21 CFR Part 600-680) cultures. A summary of the file on each source animal must be available to the facility that processes/manufactures the end product. Diagnostic microbiological tests must be based on the OIE's Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (available at the following URL address: http://www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/).

The **virological safety** of tissue largely rests on:

- donor selection and the absence of initial contamination;
- the virological tests carried out at the time of donation;
- the conditions of virus inactivation.

The risk of infection during the processing phase must be minimised at various points by means of (a combination of) methods, such as mechanical cleaning, chemical decontamination, gas sterilisation and/or physical sterilisation procedures (SHC 8785, 2012).

The **microbiological safety** of the end product is based on:

- the selection of source animals and absence of initial contamination;
- management and control of contamination factors throughout the process;
- wherever applicable to specific product types, validated rules for decontamination, sterilisation or inactivation during processing of the raw material;
- microbiological tests for aerobic and anaerobic germs as well as fungi and yeast, which are carried out at various points during the process. If risk factors are already present, it is advisable that extra tests be carried out to trace mycobacteria in the end product.

The microbiological tests must be carried out on:

- source or incoming material;
- material immediately prior to final packaging;
- and wherever applicable, following a decontamination or sterilisation step (direct test or test of control product).

Various validated microbiological control procedures might be considered, as is the case with HTC, including decontamination by antibiotics, irradiation or other physicochemical procedures. These procedures must be adapted to suit the end product and be described in a detailed validation procedure that includes the rationale for the adaptation (SHC 8716, 2013).

The **parasitic safety** of the product is based in the first place on:

- donor selection, choice of country of origin and absence of initial contamination;
- parasite and serologic testing at the time of donation;
- tests for contamination when the material was harvested;
- the means of parasite inactivation.

The risk of infection during the processing stage is lowered at various points through (a combination of) different methods, such as mechanical cleaning, chemical decontamination, gas sterilisation and/or physical sterilisation processes (SHC 8785, 2012).

In the case of **prions,** the safety of the end product is based largely on the selection of source animals from a country of origin in which the BSE status presents a negligible or controlled risk. A list of the status per country and region can be found at the following URL address: http://www.oie.int/en/animal-health-in-the-world/official-disease-status/bse/list-of-bse-risk-status/. Procedures for protection for inactivation, by which the prion load is reducible, may be worth considering for some products.

Whichever technique is used, it must be one approved by the World Health Organisation, i.e.:

- treatment with sodium hydroxide, 1M, for at least 1 hour at 20°C;
- treatment with sodium hypochlorite with 2% free chlorine for at least 1 hour at 20°C;
- autoclave sterilisation between 134°C and 138°C for at least 18 minutes.

The techniques must be described in a detailed and validated procedure.
If a different procedure is used, it must be based on an evaluation of specific and convincing studies. Such procedures must be reported to the competent authority beforehand.

Several procedures can currently be followed to minimise the risk of transmitting pathogens, such as ethylene oxide, ethanol, propylene oxide, gamma radiation, and E-beam.

It is up to the manufacturer to draw up a list of the relevant pathogenic agents to be traced and to demonstrate that they are absent.

3.4.4.2. Traceability

Traceability means the ability to locate and identify all relevant information concerning the animal tissues and cells as well as the products and materials that come into contact with the animal tissues and cells, invasive devices or implants of animal origin throughout the procedure. The authorities and responsibilities of the animal tissues and cells responsible person are on a par with those of the human tissues and cells responsible person. They are set out in Appendix 2 of the present recommendations.

A. Encoding

A simple system to identify the source animal by means of a unique code for every donation and for any animal tissues and cells must be introduced. When several preparations or products are made from the same source animal, a unique batch number for each preparation/fabrication can be used as a clear link to the unique donation identification number.

The encoded data must be kept in a dedicated register.

The facilities will store the written or electronic data needed to guarantee full traceability through all the stages, for a period of at least 30 years (but no longer than 50 years) from:

a) either clinical use of the invasive devices and implants of animal origin in human beings;
b) or distribution with a view to a potential use other than that referred to in item a);
c) or destruction of the animal tissues and cells or invasive devices and implants of animal origin.

This information must be kept at the facility that obtains the material immediately after procurement.

B. Distribution of invasive medical devices and implants of animal origin

Besides the information given on the shipping labelling when the products are distributed, the products must always come with a leaflet containing relevant information on the invasive devices and implants, the animal tissues and cells used and any information essential to their use.

Most importantly, this documentation must contain information on:

- the distribution date for the invasive medical devices and implants of animal origin;
- the release of the product;
- a description of the products (quantitative data, morphological data, functional data);
- viral, bacteriological, mycological safety and TSE data;
- the composition of the preservation medium and the presence of any potentially toxic residue (antibiotics, ethylene oxide, etc.);
- recommendations on temporary storage where relevant;
- directions for use (opening the packaging, thawing and/or reconstitution, processing, etc.);
- the storage conditions and maximum storage time after opening the packaging.

The file will also contain an information form (leaflet). This documentation is intended for the surgeon who will perform the implant and must be kept in the recipient's medical file.

C. *Follow-up of invasive medical devices and implants of animal origin after distribution/biovigilance*

The manufacturers are responsible for the followup of the invasive medical devices and implants of animal origin after distribution, the materiovigilance and vigilance. They must refer to the correct legislation and on the appointed supervisory institution, in this case the FAMHP.

"Materiovigilance"[5] is the study and monitoring of incidents that might result from the use of medical devices. It enables dangerous devices to be withdrawn from the market and allows faults in medical devices to be traced and eliminated with a view to improving the quality of the devices and safety for the patients and users.
The relevant laws and regulations concerning medical devices and active implantable medical devices describe the measures to be taken in the event of accidents in the territory of Belgium. Every hospital now has a Committee for Medical Material (CMM), the composition and duties of which are determined by law (RD 2007). The committee's duties include the compulsory registration and supervision of implants and establishment of guidelines in relation to traceability.

To guarantee "vigilance"[6], it is necessary that certain required information on the implant and the recipient be kept, namely:

- recipient's name and date of birth;
- place, date, type of operation and/or referral for implantation;
- name of the surgeon responsible for implantation;
- side effects, serious adverse events or reactions, and/or problems as a result of the implantation.

The required information could be provided in the context of the CMM's hospital traceability system.

Side effects and serious adverse events and reactions ascribable to the quality or safety of the tissues and cells of animal origin must be investigated and evaluated.
Wherever relevant, including cases of disease or infection transmission by these tissues and cells of animal origin, the necessary measures must be taken, i.e.:

- immediate reporting of serious reactions to the competent authority - in this case the FAMHP;
- measures related to the traceability requirements (information from the implantation centres and harvesting centres where applicable);
- recall of tissues and cells of animal origin already distributed but not yet used;
- non-distribution of remaining tissues and cells of animal origin affected and recall of those in temporary storage or which have been preserved;
- measures to immediately isolate the tissues of animal origin;
- evaluation of anticipated causes during the procedure and introduction of corrective and/or preventive measures where applicable;

[5] http://www.fagg-afmps.be/en/human_use/health_products/medical_devices_accessories/
[6] http://www.fagg-afmps.be/en/human_use/health_products/human_body_material/

- follow-up of and report on the measures taken for the competent authority by completing the forms provided by the competent authority (FAMHP).

It would seem appropriate to collect additional information concerning the clinical follow-up of the recipient. This information could be used in a retrospective evaluation of the clinical results. It might therefore be one of the essential elements in validating and evaluating the processing, preservation and storage procedures described by the manufacturer of the implants.

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5. APPENDIX 1 - Definitions

5.1. Appendix 1: *definitions*

Acellular biomaterial: in biology, the **cell** is the smallest part of any organism or living being to contain all of the organism's genetic information. "Decellularisation" is the removal of cells, e.g. one of the purposes of decellularisation when making "*matrices or scaffolds*" is to remove the cellular material and its residual debris while leaving the essential structural components and mechanical integrity of the remaining extra-cellular matrix intact.

Active medical device: any medical device that relies, for its functioning, on a source of electrical energy or any source of power other than that directly generated by the human body or gravity.

Active implantable medical device: any active medical device that is intended to be totally or partially introduced, surgically or medically, into the human body or by medical intervention into a natural orifice, and which is intended to remain after the procedure (RD 1997).

Processing: any operation undertaken during the preparation, manipulation, preservation and packaging of animal tissues and cells intended for human applications

Serious adverse event: means any untoward occurrence associated with the procurement, testing, processing, storage and distribution of tissues and cells that might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions for patients or which might result in, or prolong, hospitalisation or morbidity (EU directive 2004/23/EC)

Serious adverse reaction: means an unintended response, including a communicable disease, in the donor or in the recipient associated with the procurement or human application of tissues and cells that is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs, hospitalisation or morbidity; (EU directive 2004/23/EC)

Medical application in human beings: the use of tissues and cells on or in a human recipient, including extracorporeal application.

Gnotobiotic: a gnotobiotic animal is an animal whose microbiological flora is "theoretically" known. In practice, the animal is bred in a closed and sterile environment. The animal is generally born by caesarean section and isolated immediately. It does not therefore contain microorganisms that have not been administered by the researchers. The term is often used to denote germ-free animals or, in other words, animals which are free of microorganisms. These animals are procured and bred as gnotobiotic animals.

Implant: any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used mainly for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease, injury or disability;

- investigation, replacement or modification of the anatomy or of a physiological process, whereby the principal intended action in or on the human body is not achieved by pharmacological, immunological or metabolic means, but may be assisted in its function by such means.

The implant is entirely or partially implanted in the human body by operative or medical means or in a natural orifice or replaces part of the epithelial tissue. It is designed to remain in place for at least 30 days after the operation. The implant can only be removed by surgical or medical operation (National Service for Health and Disability Insurance nomenclature - Article 35 of the nomenclature).

Implantable medical device: any device that was designed:

- to be wholly implanted in the human body; or
- to replace an epithelial surface or the surface of the eye by means of a surgical operation and was designed to remain in place after the operation.

Any device that was designed to be partially inserted in the human body by means of a surgical operation and to remain in place for at least 30 days after the operation is also considered an implantable device (RD 1999).

Invasive medical device: a medical device that penetrates the body partially or entirely, either through an orifice in the body or through the surface of the body (National Service for Health and Disability Insurance nomenclature - Article 35bis of the nomenclature.

Long-term invasive medical device: a medical device that penetrates the body partially or entirely, either through an orifice in the body or through the surface of the body, and is usually expected to operate for more than 30 days of continuous use.

Medical device: any instrument, device or apparatus, any software or substance or any other article that is used alone or in combination, including any accessory and the software necessary for its proper operation, and intended specially by the manufacturer to be used for diagnostic and/or therapeutic purposes and intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease;
- diagnosis, monitoring, treatment, alleviation or compensation of an injury or disability;
- examination, replacement or modification of the anatomy or of a physiological process;
- controlling fertility;

whereby the principal intended action in or on the human body is not achieved by pharmacological, immunological or metabolic means, but may be assisted in its function by such means.

Non-living biomaterial, synonym avital biomaterial: the result of a procedure applied to biomaterial in which all biological functions are switched off, possibly by removing the cells (including the genetic material in the cell core). E.g. chemical fixation renders any cellular material present avital.

Preservation: the use of chemical or biological substances, changes in environmental conditions or other means during processing to protecting the quality of the material or preventing or delaying its biological or physical degradation.

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Specific pathogen free (SPF): a laboratory animal is free of specific pathogenic organisms (Specific pathogen free, SPF) if it can be guaranteed that it is not infected by specifically traced microorganisms/viruses. The term can only be used in relation to the list of traced pathogenic agents for which the animal is declared “SPF”.

Traceability: the ability to locate and identify the tissues and cells at every stage of the process, from procurement to distribution, with a view to utilisation or destruction and to do so during processing, testing and storage. This includes the ability to identify the source animal as well as the organisation(s) or production unit(s) that received, processed or stored the tissues and cells, as well as the recipients in the hospitals at which the tissues and cells are utilised. It also involves the possibility of locating and identifying all the relevant information relating to products and materials that came into contact with the tissues and cells during the process.

Harvesting: the operation by which tissues and cells are extracted from the body of the animal.

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5.2. Appendix 2: human tissues and cells responsible person (SHC 8716, 2013)

He/she keeps current with the latest developments in medical science in those areas affecting the activities of the HTC facility and he/she passes this information on to the people who extract tissues and cells and/or use the allografts.

The HTC responsible person is responsible for the HTC facility and consequently for all of the processes that take place there. He/she may delegate certain duties, but retains overall responsibility. Duties may only be delegated to people with (bio)medical or paramedical qualifications who have followed a course of training in relation to the delegated duty. The rules of delegation must be described in a procedure.

If the responsible person is temporarily absent, an appointed replacement, with similar qualifications and preferably some practical experience in HTC management, will be delegated the duties and responsibilities of the facility's HTC responsible person.

Pursuant to the legislation and implementing orders on HTC (Law of 19/12/2008; RD 2009), the HTC responsible person is responsible for a number of duties in the HTC facility.
A summary of the duties specified in different parts of the legislation is given below. Wherever possible, they have been grouped according to activity type.

Organisation and management

- Perform the duties for which the facility has received accreditation, such as selection of donors, assessment of HTC clinical data, interaction with clinical users, etc.;
- Monitor the quality of the HTC and the quality and safety of operations carried out with HTC in the facility or carried out by a third party;
- Grant permission[7] to an intermediary organisation to:
  - supply HTC with a view to their application in human beings, or the industrial manufacture of products, or its use in science;
  - export HTC.
- Establish a discontinuation procedure.

Encoding and traceability

- Issue an identification code to the donor and the donated HTC when the material is harvested or at the latest when it is received at the facility;
- Safeguard the key to the encoding system;
- Facilitate the traceability of HTC from receipt to distribution, donor to recipient and vice versa. In cases where material is transferred between banks or intermediary organisations, the responsible person is responsible for ensuring the continuity of the traceability system. When HTC are supplied to another hospital, it is not the HTC responsible person, but rather the hospital in question, that takes responsibility for ensuring traceability, from receipt to implantation of the HTC in the recipient.

[7] This duty is only relevant in the case of a HTC bank responsible person.

Harvesting of HTC

- Inform the donor (or his/her representative as set out in the legislation concerning patient rights) if, in respect of a procedure carried out on the HTC or as a result of using the donor's HTC, analyses yield significant information on the donor's state of health. This is generally done by the treating physician;
- File the written certificate of permission and record the subject and scope of the permission (obtained via the surgeon responsible for extracting the material) in the living donor's donor file as well as any requests for information or changes to permission;
- A record must also be kept of any changes to permissions;
- File the tissue harvesting report and any other documentation relating to the donor.

Release and distribution

- Verify in writing the acceptance/release or refusal of HTC;
- Ensure that HTC are not supplied for a use other than that for which the permission was granted;
- Obtain recommendations from the ethics committee before supplying HTC for secondary use;
- Check HTC imported or transferred from another Member State of the European Union (EU) for conformity with the Royal Decree (RD) on stipulated quality (RD 2009);
- Gather information in the exceptional case that HTC are imported or transferred and are intended purely for export or further transfer. In that case, the information obtained must offer sufficient guarantees that the imported or transferred material is genuinely intended solely for export or transfer;
- Authorise an exception to the selection criteria set out in the RD on the basis of a documented risk analysis;
- Set up and manage a documented system confirming that the HTC satisfy all the safety and quality requirements for release and distribution;
- Set up a documented risk assessment system to ascertain whether HTC that do not satisfy the quality criteria can be considered fit for release.

Serious Adverse Event (SAE) / Serious Adverse Reaction (SAR)

- Report to the FAMHP every SAE that occurs when assessing donor suitability, during extraction or during any other operation involving HTC in the facility and every SAR that occurs in a living donor and provide a report of its causes and effects;
- Report to the FAMHP every SAR observed in a recipient and every SAE reported by a hospital to the HTC facility;
- Report the measures taken when other HTC are distributed;
- Report the conclusions of the investigation;
- Report the effects on other tissues/organs: in the event that the reaction or event is likely to affect the recipients of organs or the recipients of HTC from the same donor, the HTC administrator must notify the transplantation coordinator and/or the HTC administrators of the other HTC facilities.

6. COMPOSITION OF THE STUDY GROUP

All of the experts participated in the study group in a ***personal capacity***. The names of the SHC experts named by RD, the members of the Committee and the Board, and the general declaration of interests of the experts are available on our website www.hgr-css.be (link: composition and operations - link: Conflicts of interest - only available in Dutch and French).

The following experts contributed to the formulation of the recommendations:

BOUTSEN-ECTORS Nadine	Medicine, anatomical pathology	KUL
HEINEN Ernst	Human histology	Univ. of Liège
LEMPEREUR Laetitia	Parasitology	
MAINIL Jacques	Infectious diseases, bacteriology	Univ. of Liège
NAUWYNCK Hans	Virology, veterinary medicine	UH Ghent
SAEGERMAN Claude	Epidemiology and risk analysis in veterinary medicine	Univ. of Liège
THIRY Etienne	Veterinary virology	Univ. of Liège
VAN GEYT Caroline	Medical-social science	UH Ghent

The role of chairperson was assured by Nadine BOUTSEN-ECTORS and the role of scientific secretary by Muriel BALTES.

The following experts approved the recommendations:

BEELE Hilde	Medicine, dermatology	UH Ghent
DELFORGE Alain	Medicine, cell therapy	ULB
DELLOYE Christian	Medicine, orthopaedic surgery	UCL
GUNS Johan	Medical-social science	UH Brussels
MUYLLE Ludo	Medicine, clinical biology	FAMHP, UH Antwerp, Univ. of Antwerp
PIRNAY Jean-Paul	Medical science	MHKA
THONON Fabienne	Reproductive medicine, embryology	UH Liège
VAN RIET Ivan	Medicine, cell therapy	UH Brussels
VANDERKELEN Alain	Medicine, general surgery	HMRA Brussels
VERBEKEN Gilbert	Biology, QA/QC/RA	MHKA

The role of administrator was filled by:

SEKKALI Belaïd	Quality Assessor	FAMHP

The role of chairperson was assured by Hilde BEELE and the role of scientific secretary by Muriel BALTES.

About the Superior Health Council (SHC)

The Superior Health Council is a federal advisory body. Its secretariat is provided by the Federal Public Service Health, Food Chain Safety and Environment. It was founded in 1849 and provides scientific advisory reports on public health issues to the Ministers of Public Health and the Environment, their administration, and a few agencies. These advisory reports are drawn up on request or on the SHC's own initiative. The SHC aims at giving guidance to political decision-makers on public health matters. It does this on the basis of the most recent scientific knowledge.

Apart from its 25-member internal secretariat, the Council draws upon a vast network of over 500 experts (university professors, staff members of scientific institutions, stakeholders in the field, etc.), 300 of whom are appointed experts of the Council by Royal Decree. These experts meet in multidisciplinary working groups in order to write the advisory reports.

As an official body, the Superior Health Council takes the view that it is of key importance to guarantee that the scientific advisory reports it issues are neutral and impartial. In order to do so, it has provided itself with a structure, rules and procedures with which these requirements can be met efficiently at each stage of the coming into being of the advisory reports. The key stages in the latter process are: 1) the preliminary analysis of the request, 2) the appointing of the experts within the working groups, 3) the implementation of the procedures for managing potential conflicts of interest (based on the declaration of interest, the analysis of possible conflicts of interest, and a Committee on Professional Conduct) as well as the final endorsement of the advisory reports by the Board (ultimate decision-making body of the SHC, which consists of 40 members from the pool of appointed experts). This coherent set of procedures aims at allowing the SHC to issue advisory reports that are based on the highest level of scientific expertise available whilst maintaining all possible impartiality.

Once they have been endorsed by the Board, the advisory reports are sent to those who requested them as well as to the Minister of Public Health and are subsequently published on the SHC website (www.shc-belgium.be). Some of them are also comunicated to the press and to specific target groups (healthcare professionals, universities, politicians, consumer organisations, etc.).

In order to receive notification about the activities and publications of the SHC, please contact: info.hgr-css@health.belgium.be.

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