EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2015. Scientific Opinion on an alternative method for the hygienic treatment of bovine colostrum through a series of filtration steps

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SCIENTIFIC OPINION

Scientific Opinion on an alternative method for the hygienic treatment of bovine colostrum through a series of filtration steps[1]

EFSA Panel on Biological Hazards (BIOHAZ)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

An alternative method to the HTST treatment (High Temperature Short Time pasteurisation at 72 °C for at least 15 seconds or equivalent pasteurisation effect achieving a negative reaction to a phosphatase test), approved for the treatment of bovine colostrum (Category 3 material), was assessed. The purpose of the alternative method, based on a series of filtration steps, is the production of Colostrinov, a product whose main ingredient is bovine colostrum, to be used for foal nutrition. Since the filtration techniques used are known to eliminate particles of the size of bacteria, fungi and protozoa from liquids, it is reasonable to assume that the microfiltration process reduces these contaminants to a level at least equivalent to the treatment required by the legislation. Owing to their small size, viruses are not retained by the mechanical effect of the filters but they may be retained by physico-chemical interactions with the surface of the filter, depending on the surface properties of the viruses and those of the filter, as well as on the properties of the surrounding liquid. From the information provided by the applicant, it cannot be concluded whether or not the microfiltration process reduces the relevant viral contaminants to a level at least equivalent to a single HTST treatment as required by the legislation.

KEY WORDS

bovine, colostrum, ultrafiltration, microfiltration, foal nutrition, Colostrinov

[1] On request from the French Competent Authority, Question No EFSA-Q-2014-00703, adopted on 4 June 2015.

[2] Panel members: Olivier Andreoletti, Dorte Lau Baggesen, Declan Bolton, Patrick Butaye, Paul Cook, Robert Davies, Pablo S. Fernández Escámez, John Griffin, Tine Hald, Arie Havelaar, Kostas Koutsoumanis, Roland Lindqvist, James McLauchlin, Truls Nesbakken, Miguel Prieto Maradona, Antonia Ricci, Giuseppe Ru, Moez Sanaa, Marion Simmons, John Sofos and John Threlfall. Correspondence: biohaz@efsa.europa.eu

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SUMMARY

Following a request from the Permanent Representation of France to the European Union (EU) (competent authority) on behalf of the French company IMV-Technologies, the European Food Safety Authority (EFSA) Scientific Panel on Biological Hazards (BIOHAZ Panel) was asked to deliver a scientific opinion on an alternative method for hygienic treatment of bovine colostrum.

Raw bovine colostrum (first milk after parturition) (Category 3 material) is considered to be raw milk as per Article 10(h) of Regulation (EC) 1069/2009, the Animal By-product Regulation (ABP). According to Point 6.3 of Section 4, Part I.B, Chapter II, Annex X of Regulation (EC) 142/2011, colostrum or colostrum products must have undergone a single HTST treatment (HTST = High Temperature Short Time pasteurisation at 72 °C for at least 15 seconds or equivalent pasteurisation effect achieving a negative reaction to a phosphatase test).

Under point 5 of Article 20 of Regulation 1069/2009 it is specified that EFSA shall assess whether the alternative method submitted ensures that risks to public or animal health are: a) controlled in a manner which prevents their proliferation before disposal in accordance with this Regulation or the implementing measures thereof; or b) reduced to a degree which is at least equivalent, for the relevant category of animal by-products, to the processing methods laid down pursuant to point (b) of the first subparagraph of Article 15(1).

The alternative method is based on a series of filtration steps for the production of Colostrinov, a product whose main ingredient is bovine colostrum. The intended use of the product, rich in immunoglobulin (Ig)G, is foal nutrition. Following a confidentiality claim, the description of the process has been edited.

The BIOHAZ Panel considered a list of main hazards potentially present in bovine colostrum: pathogenic and non-pathogenic bacteria, pathogenic viruses, pathogenic fungi and pathogenic protozoa. Since the filtration techniques used are known to eliminate particles of the size of bacteria, fungi and protozoa from liquids, it is reasonable to assume that the microfiltration process reduces these contaminants to a level at least equivalent to the treatment required by the legislation.

However, no information is provided in the application on the potential reduction in pathogenic viruses in colostrum after applying the alternative method. The data provided in the literature attached to the application refer only to bacteriophages. The applicant did not perform an experiment with colostrum containing, or spiked with, appropriate indicators of the relevant pathogenic viruses.

Owing to their small size, viruses are not retained by the mechanical effect of the filters but they may be retained by physico-chemical interactions with the surface of the filter, depending on the surface properties of the viruses and those of the filter, as well as on the properties of the surrounding liquid. Therefore, a description of the characteristics of the filters used for the microfiltration process is essential.

From the information provided by the applicant, it cannot be concluded whether or not the microfiltration process reduces the relevant viral contaminants to a level at least equivalent to a single HTST treatment as required by the legislation. Although a detailed Hazard Analysis and Critical Control Points (HACCP) Plan was provided, some improvements are necessary. In particular, a full list of hazards should be provided and microfiltration should be identified as a Critical Control Point (CCP) for virus reduction. In this context, the characteristics of the micro-filters should be clearly specified in the description of the process. The control of the filtration process and maintenance of the equipment are essential for the efficacy of any method based on filtration.

The efficacy of the alternative method should be validated with colostrum artificially contaminated with suitable test-viruses, selected according to their size and surface properties, and not to their

thermal resistance. Only test-strains should be used for which approved quantitative laboratory methods are available comparable to those described for testing disinfectants.

The cold chain, as described in the application, should be maintained at all times in order to ensure the safety of the product. Systems should be in place to ensure the safe disposal of wastewater.

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BACKGROUND AS PROVIDED BY THE FRENCH COMPETENT AUTHORITY

On 01 October 2014, The European Food Safety Authority (EFSA) received from the Permanent Representation of France to the EU (competent authority) the application (mandate and technical dossier) under Regulation (EC) No 1069/2009[4] and Regulation (EU) No 142/2011,[5] referring to the request for evaluation of an alternative method for hygienic treatment of colostrum, submitted by IMV-Technologies.

The application dossier includes a number of supporting documents which have also been listed in the enclosed Index.

TERMS OF REFERENCE AS PROVIDED BY THE FRENCH COMPETENT AUTHORITY

The French competent authority asked EFSA to assess an alternative method for hygienic treatment of bovine colostrum (Category 3 material) via microfiltration, intended to be used for foal nutrition, according to Article 20 of Regulation (EC) 1069/2009 and Annex VII of Regulation (EU) 142/2011. In point 5 of Article 20, it is specified that EFSA shall assess whether the method submitted ensures that risks to public or animal health are:

a) controlled in a manner which prevents their proliferation before disposal in accordance with this Regulation or the implementing measures thereof; or

b) reduced to a degree which is at least equivalent, for the relevant category of animal by-products, to the processing methods laid down pursuant to point (b) of the first subparagraph of Article 15(1).

The proposed method is an alternative to the approved one. According to Point 6.3 of Section 4, Part I.B, Chapter II, Annex X of Regulation (EC) 142/2011, colostrum or colostrum products must have undergone a single HTST treatment (HTST = High Temperature Short Time pasteurisation at 72 °C for at least 15 seconds or equivalent pasteurisation effect achieving a negative reaction to a phosphatase test).

[4] 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), OJ L 300, 14.11.2009, p. 1–33, as last amended.

[5] Commission Regulation (EU) No 142/2011 of 25 February 2011 implementing Regulation (EC) No 1069/2009 of the European Parliament and of the Council laying down health rules as regards animal by-products and derived products not intended for human consumption and implementing Council Directive 97/78/EC as regards certain samples and items exempt from veterinary checks at the border under that Directive, OJ L 54, 26.2.2011, p. 1–254, as last amended.

ASSESSMENT

1. Introduction

The terminology used in this assessment conforms to the 'Statement on technical assistance on the format for applications for new alternative methods for animal by-products' (EFSA BIOHAZ Panel, 2010). The assessment considers only biological hazards. Other hazards (e.g. physical, chemical or radiological) are not considered.

The assessment of the application received was performed taking into account the criteria laid down in Article 20, point 5 of Regulation (EC) 1069/2009 (the Animal By-Products (ABP) Regulation). The purpose of the alternative method is the production of Colostrinov, a product whose main ingredient is bovine colostrum, to be used for foal nutrition.

2. Full description of the process

According to Annex VII to Regulation (EU) 142/2011, the applicant is required to provide a full description of the process to be assessed.[6]

The following text, along with Figure 1, summarises the information provided.

2.1. Collection

The animals that contribute to the production of colostrum are subjected to the same requirements as those that produce milk for human consumption. The colostrum is collected by the producers into clean, disinfected, milking machine pots dedicated to this use. The pots are packaged immediately in disposable, double-lined, food-grade plastic bags and then frozen at – 18 °C in freezers made available to the producers. A label containing a producer-specific bar code is placed on each bag.

The colostrum is transferred frozen taking the necessary precautions either to a processing plant for dairy products (company 1) licensed under Regulation (EC) 853/2004[7] where it is stored in a freezer (at − 18 °C) dedicated to colostrum harvesting, or to a dedicated freezer in a cold store company (company 2).

2.2. Thawing and skimming

The process of production starts with the raw material, i.e. frozen bovine colostrum at − 18 °C. According to the application, frozen colostrum is quickly thawed in specifically designed equipment in less than 60 minutes; the colostrum temperature is increased from – 18 °C to 15 °C. However, there is an inconsistency between the application dossier and the Hazard Analysis and Critical Control Points (HACCP) plan in relation to the thawing process. This is further discussed in section 6 (HACCP plan) of this Scientific Opinion.

From the colostrum thawing stage onwards, a representative sample is taken from all of the unprocessed colostrum used in order to detect the presence of salmonellae.

The colostrum is then skimmed at 38 °C in a skimmer dedicated to this purpose and the cream is then disposed of in accordance with the ABP Regulation.

2.3. Filtrations

The skimmed colostrum is transferred into the microfiltration operating unit (0.1 µm) feeding tank, which is located in another room at positive pressure. The permeate, which is rich in immunoglobulin (Ig)G, is transferred to a frontal filtration unit (0.45 µm) and then to the ultrafiltration feeder tank. The

[6] This section has been edited following a confidentiality claim made by the applicant.
[7] Regulation (EC) No 853/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific hygiene rules for the hygiene of foodstuffs. OJ L 139, 30.4.2004, p. 55–151.

ultrafiltration retentate remains in the ultrafiltration unit until its refractive index reaches 25 %. The final product goes through another filtration (0.22 µm) at a later stage (see Section 2.5).

There is no description in the application on the characteristics of the filters used for the microfiltration and ultrafiltration. There are no details either on the protocol for maintenance and verification of the filters except the verification of the 0.45 µm filter integrity by measurement of the bubble point, the visual monitoring of absence of leakage and the verification of the integrity of the filters before and after the production process. The corrective action is the replacement with a new filter and the destruction of the deteriorated one.

According to the HACCP Plan, cleaning and disinfection of dedicated equipment for production of colostrum, namely, filtration units, filters, circuits and trays, is done as a preventative measure to avoid microbiological contamination. The microfiltration filter is steam sterilised and the filter is autoclaved prior to re-use. In order to avoid microbiological and chemical contamination, cleaning-in-place is done including rinsing and use of cleaning agents and disinfectants accredited for foodstuff use.

2.4. Cooling

When the refractive index of the ultrafiltration retentate reaches 25 %, a valve opens automatically to release it into a continuously-mixed cooling tank where it reaches temperatures between 2 °C and 10 °C. The tank is sealed and stored in a cold room (4 °C) until it is transported for one hour to the next site (IMV-Technologies). There is no information on the length of time that the colostrum is kept in the cold room or on the transport temperature.

2.5. Freezing

As soon as it is received at IMV-Technologies, the tank is stored in a cold room (4 °C) until its contents are used, less than 48 hours after receipt. The concentrated serocolostrum is then filtered through 0.22 µm filters before aliquots are dispensed into disposable bags which are placed on stainless steel trays. There are no details of the material with which the disposable bags are manufactured. The serocolostrum is then frozen. All of these procedures are carried out in an ISO8-compliant room.

2.6. Freeze-drying

The frozen bags are transported to a freeze-drying company (company 3) where they are transferred immediately to large bags and then to freezers (at − 18 °C) equipped with temperature probes and alarms. On the day of freeze-drying, the bags are weighed, opened and positioned on freeze-drying shelves, which have been previously cleaned and disinfected. No further details are provided on these procedures.

After a 72-hour cycle, the lyophilisate (also called the dry extract) is removed from the freeze-dryer and packaged in farming-foodstuff certified grade disposable polyethylene bags. These packages, which each weigh 5 kg, are then packaged in a large (double-lined) bag. All of these procedures are carried out in an ISO8-compliant room. The 5 kg packs are sent to IMV-Technologies within 48 hours of production.

2.7. Packaging of the commercial product

The 5 kg packs are stored in a cold room at 4 °C as soon as they are received. A 174 g mass of lyophilisate followed by 90 g of powdered milk are added into a new 1 000 mL polyethylene terephthalate (PET) bottle. The bottle is then closed with the PET top. All of these procedures are carried out in an ISO8-compliant room. Each bottle is fitted with a feeding teat for marketing. The commercial product must be stored in a cool and dry place and away from light (at temperature not exceeding 30 °C) for a maximum of one year after packaging.

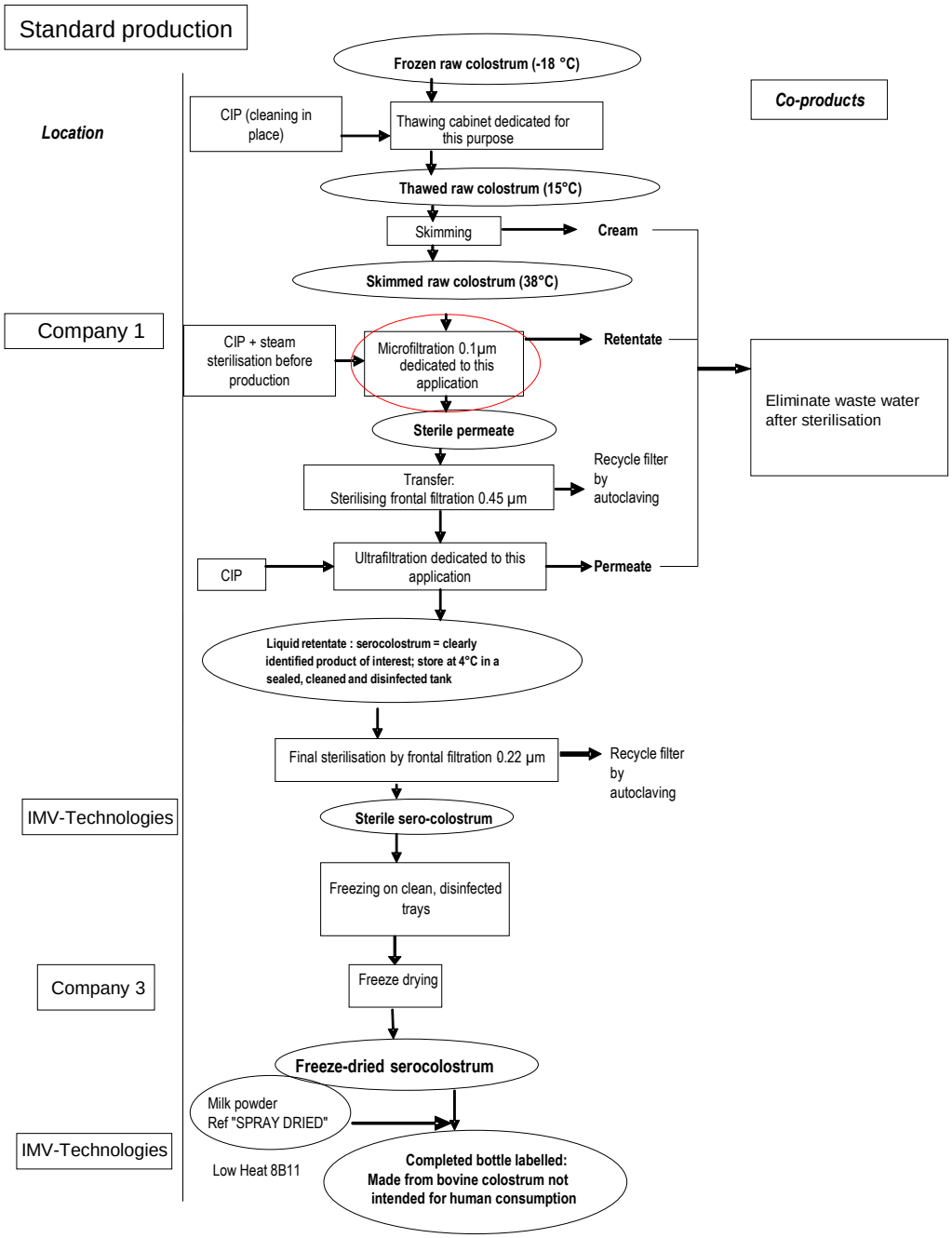

Figure 1: Summary diagram of the production process as proposed by the IMV-Technologies excluding the confidential steps

3. Full description of the material to be treated

Raw bovine colostrum (first milk after parturition) (Category 3 material) is considered to be raw milk as per Article 10(h) of Regulation (EC) 1069/2009 (the ABP Regulation). Colostrum means 'the fluid secreted by the mammary glands of milk-producing animals up to three to five days post parturition that is rich in antibodies and minerals, and precedes the production of raw milk', according to Regulation (EC) 853/2004, Annex III, Section IX, as amended. The health requirements for raw milk and colostrum production are the same, as per Chapter I, Section IX, Annex III of Regulation (EC)

853/2004, as amended by Regulation (EC) 1662/2006.[8] Milk, milk-based products, milk-derived products, colostrum and colostrum products require different certificates for import into the European Union (EU) from third countries (non-EU members), as stated in the Regulation (EC) 142/2011[9] Annex XV, Chapters 2 (A) and 2 (B).

According to point 6 Section 4 Part I.B, Chapter II, Annex X of Regulation (EC) 142/2011, colostrum and colostrum products must:

6.1 be obtained from bovine animals kept on a holding on which all bovine herds are recognised Officially Tuberculosis-Free, Officially Brucellosis-Free and Officially Enzootic-Bovine-Leukosis free as defined in Article 2(2)((d), (f) and (j)) of Directive 64/432/EEC;[10]

6.2 have been produced at least 21 days before shipping (during that period no case of foot-and-mouth disease must have been detected in the Member State of origin);

6.3 have undergone a single HTST treatment (high-temperature short-time pasteurisation at 72 °C for at least 15 seconds or equivalent pasteurisation effect achieving a negative reaction to a phosphatase test);

6.4 comply with the requirements set out in point 4 of Part I.B:

4.1 after completion of the processing, every precaution must be taken to prevent contamination of the products;

4.2 the final product must be labelled so as to indicate that it contains Category 3 material and is not intended for human consumption and it must be: a) packed in new containers; or b) transported in bulk in containers or other means of transport that before use were thoroughly cleansed and disinfected.

With regards to the assessment, Article 20 of Reg. 1069/2009 specifies that the method submitted for approval must reduce the public or animal health risks to a degree at least equivalent, for the relevant category of animal by-products, to the processing methods laid down pursuant to point (b) of the first subparagraph of Article 15(1). The laid-down processing method for colostrum is the HTST as described above in point 6.3.

4. Hazard identification

A comprehensive list of pathogens that could be present in colostrum was not provided by the applicant. The EFSA Panel on Biological Hazards (BIOHAZ Panel) considered the list of main hazards potentially present in bovine colostrum (those mentioned by the applicant are highlighted with an asterisk) (Peterson, 1965; Kawakami et al., 1966; Richardson, 1970; Ménard et al., 1983; Timoney et al., 1988; Watts, 1988; Lorenz et al., 1998; Waage et al., 1999; Pardo et al., 2001; Mukherjee et al., 2004; Izumi et al., 2006; Biesenkamp-Uhe et al., 2007; Barlow et al., 2008; Cervinkova et al., 2013; EFSA BIOHAZ Panel, 2015).

The hazards included in the list have been compiled from those reported in the literature as excreted in bovine milk, regardless of their excretion in equine milk or their pathogenicity for equines. It was

[8] Commission Regulation (EC) No 1662/2006 of 6 November 2006 amending Regulation (EC) No 853/2004 of the European Parliament and of the Council laying down specific hygiene rules for food of animal origin. OJ L 320, 18.11.2006, p. 1–10.

[9] Commission Regulation (EU) No 142/2011 of 25 February 2011 implementing Regulation (EC) No 1069/2009 of the European Parliament and of the Council laying down health rules as regards animal by-products and derived products not intended for human consumption and implementing Council Directive 97/78/EC as regards certain samples and items exempt from veterinary checks at the border under that Directive. OJ L 54, 26.2.2011, p. 1–254.

[10] Council Directive 64/432/EEC of 26 June 1964 on animal health problems affecting intra-Community trade in bovine animals and swine. OJ L 121, 29.7.1964, p. 1977–2012.

decided not to include equine pathogens since the reduction of the pathogen load in the raw material as evidence of the effectiveness of the method can only be assessed with pathogens present in bovine colostrum. Moreover, while the intended use of Colostrinov is foal nutrition, its administration to other species susceptible to pathogens included in the list cannot be excluded.

4.1. Bacteria

Bacterial pathogens, for example*:*

- *Arcanobacterium pyogenes*
- *Bacillus cereus*
- *Brucella abortus*
- *Campylobacter* spp. (thermophilic)
- *Chlamydophila abortus*
- *Clostridium perfringens*
- *Corynebacterium* spp.
- *Coxiella burnetii*
- *Histophilus somni*
- *Klebsiella* spp.
- *Listeria monocytogenes**
- *Mycoplasma bovis*
- *Mycobacterium bovis*
- *Mycobacterium* spp. *(*Atypical mycobacteria e.g. *M. phlei, M. fortuitum, M. smegmatis, M. avium, M. chelonae)*
- *Salmonella* spp.* (non-typhoid)
- Shigatoxin-producing *Escherichia coli (*STEC*)**
- *Staphylococcus aureus**
- *Streptococcus agalactiae*
- *Streptococcus equi* subsp. *zooepidemicus*
- *Yersinia enterocolitica*
- *Yersinia pseudotuberculosis*

Besides pathogenic bacteria, a variety of non-pathogenic bacteria may cause spoilage of the final products under certain conditions, or be used as hygiene indicators. These include:

- coliforms*
- *Enterobacteriaceae*
- *Pseudomonas* spp.
- *Streptococcus* spp.
- *Bacillus* spp.
- *Clostridium* spp.

4.2. Pathogenic viruses

- Bovine enterovirus
- Bovine herpesvirus 1
- Bovine herpesvirus 4
- Bovine immunodeficiency virus
- Bovine leukemia virus
- Bovine morbillivirus
- Bovine papillomavirus
- Foot-and-mouth disease virus
- Parainfluenza 3 virus
- Parapoxvirus bovis
- Tick-borne encephalitis virus

- Vesicular stomatitis virus
- Bovine viral diarrhoea virus

The viruses in the list above are those described in the literature as being excreted by the mammary gland of bovines in milk (Straub and Kielwein, 1965; Timoney et al., 1988; Watts, 1988; Wellenberg et al., 2002; Jost and Billington, 2005; Haskell, 2011; Franco et al., 2013; EFSA BIOHAZ Panel, 2015). Of those included in the list, the Tick-borne encephalitis virus (Sellon and Long, 2007; McLachlan and Dubodi, 2011), the Vesicular stomatitis virus (Sellon and Long, 2007; McLachlan and Dubodi, 2011) and the Bovine papillomavirus (Bocaneti et al., 2014) are known to be pathogenic for equines. It cannot be ruled out that additional viruses may be found in colostrum during the septicaemic phase of an infection, due to the large content number of cells and large amount of blood-derived proteins in colostrum. Besides pathogenic viruses in the colostrum itself, a variety of viruses of faecal origin may contaminate the final product under certain conditions. Therefore, a secondary risk may be considered, e.g. due to the presence of:

- Bovine rotavirus
- Bovine parvovirus
- Bovine coronavirus

4.3. Pathogenic fungi

- *Candida albicans*
- *Prototheca zopfii*

A variety of non-pathogenic fungi may cause spoilage of the final products under certain conditions.

4.4. Pathogenic protozoa

- *Cryptosporidium parvum*
- *Toxoplasma gondii*

Viruses and fungi were not considered by the applicant in its experimental assessment of risk reduction and this is one of the problems of the application. Only some bacteriophages are mentioned as test organisms in the literature review attached to the application.

Further details on potential hazards present in bovine raw milk are provided in the EFSA's scientific opinion on the public health risks related to the consumption of raw drinking milk (EFSA BIOHAZ Panel, 2015).

5. Level of risk reduction

5.1. Pathogenic bacteria

The type of filters used in the process can reduce the level of bacterial pathogens to at least the same extent as the HTST pasteurisation process, as required in Regulation (EC) 142/2011, Annex X, Chapter II, Section 4 Part I.B, point 6, whereby colostrum and colostrum products must have undergone a single HTST treatment.

The applicant carried out microbiological tests on five lots of finished serocolostrum product. The results for the five lots of product showed a reduction in total mesophilic counts from 1.2×10^7 to below the detection level (less than 100 CFU/mL) after microfiltration. The absence of *Salmonella* in 25 g of sample was reported in both the raw material and the end product. No experiments were performed with product spiked with indicator microorganisms in order to determine the actual level of reduction of a particular bacterial population. Nevertheless, since the filtration techniques used are known to eliminate particles of the size of bacteria from liquids, it is reasonable to assume that the microfiltration process reduces bacterial contaminants to a level at least equivalent to the treatment

required by the legislation. This equivalent reduction has been reported elsewhere (Saboya and Maubois, 2000, as provided by the applicant).

5.2. Pathogenic viruses

The applicant reports the absence of bovine viral diarrhoea and of infectious bovine rhinotracheitis in five lots of finished serocolostrum product and the absence of equine coronavirus and equine rotavirus in the final product. However, no information is provided in the application on the potential reduction in pathogenic viruses in colostrum after applying the alternative method. The data provided in the literature attached to the application refer only to bacteriophages. The applicant did not perform an experiment with colostrum containing, or spiked with, appropriate indicators of the relevant pathogenic viruses.

Owing to their small size, viruses are not retained by the mechanical effect of the filters but they may be retained by physico-chemical interactions with the surface of the filter, depending on the surface properties of the viruses and those of the filter, as well as on the properties of the surrounding liquid. Therefore, a description of the characteristics of the filters used for the microfiltration process is essential. Data on the effectiveness of HTST treatment on virus reduction in the scientific literature is limited. HTST is not adequate to eliminate foot-and-mouth disease virus (FMDV) in milk completely (Cunliffe et al., 1979; Tomasula and Konstance, 2004) as shown in different studies. For example, HTST achieved a 4 $\log_{10}$ reduction of FMDV in bovine milk, although it did not completely remove infectivity (Aly and Gaber, 2007; Tomasula et al., 2007). Similar findings were reported by Donaldson (1997) and Ryan et al. (2008) with a 5 $\log_{10}$ reduction. HTST was also found to only partially inactivate poliovirus type 1 (Strazynski et al., 2002). In a study in human milk, HTST pasteurisation is highly effective against some lipid enveloped viruses of pathogenic potential in humans, with limited or no inactivation observed for some non-lipid enveloped viruses (Terpstra et al., 2007). In addition, according to Escudero-Abarca et al. (2014), milk pasteurisation may not be stringent enough to eliminate Snow Mountain virus (SMV), and perhaps other prototype human norovirus (HuNoV).

It must be kept in mind that the physico-chemical properties of bacteriophages may be different from those of viruses of warm-blooded animals. Even within a particular species of viruses, surface-properties may be highly variable, and it is essential to use a conservative indicator virus or bacteriophage. The high organic content of colostrum is expected to interfere with the efficient adsorption of viruses in the filters.

Certain steps of the manufacturing process[11] may modify the viral load and therefore may also have an impact on the efficacy of the process to reduce the level of viruses. This impact could not be determined based on the information provided.

From the information provided by the applicant, it cannot be concluded whether or not the microfiltration process reduces the relevant viral contaminants to a level at least equivalent to a single HTST treatment as required by the legislation.

6. HACCP Plan

Although a detailed HACCP Plan was provided, some improvements are necessary:

- A comprehensive list of pathogens that could be present in bovine colostrum should have been provided.

- Despite the fact that the microfiltration stage of the manufacturing process is the key and only process of the alternative method that, according to the applicant, should remove viruses from the product, no critical control point (CCP) is identified at this stage for viruses. In particular, the last filtration before the freezing stage uses a 0.22 µm filter that retains bacteria but not

[11] Described in paragraphs 2 and 4 of Section 3 of Annex 6 of the application which is confidential information.

viruses. The filtration described in the freezing stage permits bacterial and fungal sterility but not viral sterility. This retention of viruses, if adequately validated, should be mentioned in the description of the filtration stages and added to the HACCP table, which should include details such as cause of failure to retain the viruses, parameters to control, preventive measures and monitoring and corrective actions. Equally the description of the protocols of use, maintenance, control of malfunctioning and lifespan of the filters should be included in the HACCP table.

- The freezing stage is considered by the applicant as a CCP for microbial contamination. The applicant should rename the stage, or subdivide it to clearly clarify that it includes the last filtration and the final packaging.

- There is an inconsistency between the application and the HACCP plan in relation to time and temperature of the thawing step. According to the application, frozen colostrum is quickly thawed in specifically designed equipment in less than 60 minutes and the colostrum temperature is increased from − 18 °C to 15 °C. However, the HACCP plan states that the bags of colostrum are placed the day before production in a cold room (at ≤ 4 °C for a maximum of 24 hours). On production day, the bags are rinsed with process water, weighed, opened, and the blocks of frozen colostrum are placed in a cabinet dedicated to this purpose. Clarity is required on this point.

- Disinfectants for cleaning-in-place should be selected from those disinfectants that are used in the veterinary field. There is no validation of the efficacy of the disinfection procedures in place in the HACCP Plan.

- The steam sterilisation of the microfiltration unit and the specification of the technical parameters to be kept should be mentioned in the monitoring details section of the HACCP table. Similarly, at the freezing stage the autoclaving of the filtration system should be mentioned.

7. Risk associated with interdependent processes

There is a detailed description of the by-products that are produced during the application of the alternative method. All by-products are intended to be 'disposed of in an authorised landfill, following processing', as per Regulation (EC) 1069/2009, Chapter II, Section 2, Article 14(c). However, no information is provided on the disposal of wastewater produced during the rinsing and cleaning of equipment.

The application involves several companies and sites. Details of transport conditions e.g. time and temperature, of raw material and intermediate products are not always available in the application. Thus, the application does not include sufficient details to ensure that the cold chain is maintained at all times.

8. Risk associated with the intended end use of the product

According to the information provided by the applicant, the final intended end use of the product is foal nutrition. However the possibility of the product being used to feed other animals cannot be ruled out. According to the information provided by the applicant, the product is clearly labelled as 'not suitable for human consumption' and 'made from bovine colostrum'.

The final product, i.e. the freeze-dried serocolostrum and the milk powder, is presented in a flask (pharmaceutical grade); it must be diluted in water. The instructions for use are shown in the packaging box. The solution must be prepared at least one hour and 30 minutes before administration to the foals. In order to prepare a bottle of Colostrinov, water at room temperature (18 to 30 °C) must be added to the bottle up to the 1 000 mL mark followed by thorough shaking until the product is

completely dissolved.[12] The feed bottle must be warmed at a maximum temperature of 37 °C in a water bath or administration. The reconstituted product must be stored at 4 °C and used within 24 hours of its preparation.

The additional risks arising from the incorporation of powdered milk by the processor and its dilution in water at room temperature by the farmer are not different from those derived from the use of any other dehydrated dairy product on the farm.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

- A comprehensive list of pathogens that could be present in bovine colostrum was not provided by the applicant. In particular, there is a lack of information on viral pathogens.
- As the filtration techniques used are known to remove particles of the size of bacteria, fungi and protozoa from liquids, it is reasonable to assume that the microfiltration process reduces these contaminants to a level at least equivalent to the treatment required by the legislation.
- A similar assumption cannot be made for viruses because of their smaller size. From the information provided by the applicant, it cannot be concluded whether or not the microfiltration process reduces the relevant viral contaminants to a level at least equivalent to the treatment required by the legislation.
- Certain steps of the manufacturing process[13] may modify the viral load and therefore may also have an impact on the efficacy of the process in reducing the level of viruses. This impact could not be determined based on the information provided.
- Although a detailed HACCP Plan was provided, some improvements are necessary. In particular, a full list of hazards should be provided and microfiltration should be identified as a CCP for virus reduction. In this context, the characteristics of the micro-filters should be clearly specified in the description of the process. The control of the filtration process and maintenance of the equipment are essential for the efficacy of any method based on filtration.
- There is no information in the application on the disposal of the wastewater produced by rinsing and cleaning equipment that has been in contact with the colostrum. The associated risk cannot therefore be assessed.

RECOMMENDATIONS

- The efficacy of the alternative method should be validated with colostrum artificially contaminated with suitable test-viruses, selected according to their size and surface properties, and not to their thermal resistance. Only test-strains should be used for which approved quantitative laboratory methods available, comparable to those described for testing disinfectants (DVG, 2015).
- The cold chain, as described in the application, should be maintained at all times in order to ensure the safety of the product.
- Systems should be in place to ensure the safe disposal of wastewater.

[12] In the section 'Intended use of the product by the user' of the HACCP Plan, it is stated that 1 000 mL flask of reconstituted Colostrinov must be administered in 4 doses, each of 250 mL.
[13] As described in paragraphs 2 and 4 of Section 3 of Annex 6 of the application which are considered confidential.

DOCUMENTATION PROVIDED TO EFSA

APPLICATION

1. Transmission CF 2014-212603 (AGRAP-RP 577/14). Note des autorités françaises à l'autorité européenne de sécurité des aliments (AESA). 29 September 2014.

2. Submission for authorisation of alternative method according to Article 20 of Commission Regulation (EU) 1069/2009 and Annex VII of Commission Regulation (EU) 142/2011. Demonstration of the safety of the proposed alternative method. Last draft: 1 April 2015. Submitted by: IMV-Technologies.

3. Confidentiality claim. Letter. 17 November 2014. Submitted by: IMV-Technologies.

4. First amendment to the confidentiality claim. Letter. 17 March 2015. Submitted by: IMV-Technologies.

5. Second amendment to the confidentiality claim. Letter. 31 March 2015. Submitted by: IMV-Technologies.

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GLOSSARY

Filtration	Separation of two or more components from a fluid stream based primarily on size differences (Cheryan, 1998)
Microfiltration	Filtration designed to retain particles in the 'micron' range, that is, suspended particles in the range of 0.1–5 μm (Cheryan, 1998)
Permeate	The fraction of a filtered feedstream that goes through the membrane and is depleted of macromolecules (Cheryan, 1998)
Retentate	The fraction of a filtered feedstream retained by the membrane and is enriched by the retained macromolecules and some of the permeable solutes (Cheryan, 1998)
Ultrafiltration	Filtration designed to retain macromolecules or particles larger than about 10–220 Å (about 0.001–0.02 μm) (Cheryan, 1998)

ABBREVIATIONS

ABP	Animal by-product
BIOHAZ Panel	EFSA Panel on Biological Hazards
CCP	Critical Control Point
CFU	Colony-forming unit
EFSA	European Food Safety Authority
EU	European Union
FMDV	Foot-and-mouth disease virus
HACCP	Hazard Analysis and Critical Control Points
HTST	High-Temperature Short-Time
HuNoV	Human norovirus
Ig	Immunoglobulin
PET	Polyethylene terephthalate
SMV	Snow Mountain virus