(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 March 2012 (08.03.2012)

PCT

(10) International Publication Number
WO 2012/030764 A2

(51) International Patent Classification:
A23C 1/08 (2006.01) *A23C 3/02* (2006.01)
A23C 1/14 (2006.01) *A23C 3/07* (2006.01)

(21) International Application Number:
PCT/US2011/049645

(22) International Filing Date:
30 August 2011 (30.08.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/378,064 30 August 2010 (30.08.2010) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,

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(54) Title: HUMAN MILK PREPARATION

(57) Abstract: This disclosure is related to human milk products, compositions and methods of making an using such compositions.

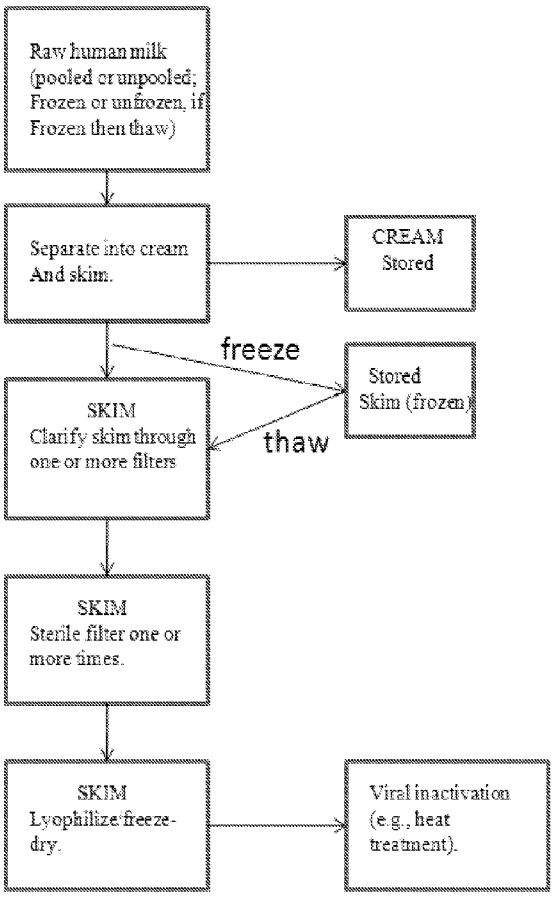

FIGURE 1

WO 2012/030764 A2

HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

HUMAN MILK PREPARATION

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 61/378,064, filed August30, 2010 the disclosure of which is incorporated herein in their entirety.

TECHNICAL FIELD

[0002] This disclosure is related to human milk products, compositions and methods of making and using such compositions.

BACKGROUND

[0003] Human milk is particularly important as a food source for preterm and full term infants because of its nutritional composition and immunologic benefits. The nutritional value of raw or conventionally-processed donor milk, however, varies and, in most instances, is not sufficient to meet the needs of preterm infants. In addition, a possibility of bacterial, viral and other contamination of raw donor milk exists. Even with pasteurization the process merely reduces bioburden to a level that is acceptable. Furthermore, heat treatment of liquid milk during pasteurization degrades and denatures important proteins and biologically relevant molecules in the human milk.

SUMMARY

[0004] The disclosure provides sterile human milk protein compositions. In one embodiment, the sterile human milk protein composition is prepared by a method comprising sterile filtering skim human milk through at least two successively smaller submicron filters to obtain a human milk protein composition; lyophilizing the human milk protein composition; and applying a viral inactivation step and/or a sterilizing process to the lyophilized human milk protein composition. In one embodiment, the skim human milk is

obtained by gravity separation for 24-36 hours or by centrifugal separation. In another embodiment, the skim human milk is clarified prior to filtration through at least one clarifying filter. In yet another embodiment, the clarifying filters comprise a micron filter or diatomaceous earth. In one embodiment, the at least one clarifying filters comprises two clarifying filters. In this embodiment, a second clarifying filter is a submicron filter. In one embodiment, the at least two submicron filters are between about 0.5 and 0.2 micron filters. In yet another embodiment, the viral sterilizing step comprises heat treatment. In one embodiment, the viral sterilizing step comprises gamma irradiation. In another embodiment, the lyophilized product comprises proteins that upon reconstitution in a liquid are biologically active. In yet another embodiment, the lyophilized product comprises at least 50% of the skim milk's lysozyme content. In yet another embodiment, the lyophilized product comprises at least 40% of the skim milk's IgA content. In yet another embodiment, the lyophilized product comprises at least 80% of the skim milk's lactoferrin content. In one embodiment, the lyophilized human milk product comprises a storage life of about 6 months or more and comprises biologically active proteins when reconstituted. In yet another embodiment, following sterile filtration the skim human milk comprises about 20-50 mg/ml protein. In one embodiment, the skim human milk comprises about 1900-2400 µg/ml lactoferrin, about 12-18 µg/ml lysozyme and/or about 1-3 mg/ml human IgA. In various embodiments, the human skim milk is non-pasteurized prior to or during filtration.

[0005] The disclosure also provides a sterile lyophilized human milk product obtained from non-pasteurized human milk

comprising biologically active human IgA, human lactoferrin, and human lysozyme proteins.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] Figure 1 shows a flow process of the disclosure.

[0007] Figure 2A-C depicts general schematics of systems of the disclosure for carrying out the method of Figure 1. (a) shows a system up through an individual vial filling step, prior to lyophilization and sterilization of the lyophilized product; (b) includes another example of filter sizes usable in the disclosure as well as demonstrating the lyophilization; and (c) shows an example utilizing a different clarification step.

DETAILED DESCRIPTION

[0008] As used herein and in the appended claims, the singular forms "a," "and," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a protein" includes a plurality of such proteins and reference to "the filter" includes reference to one or more filters, and so forth.

[0009] Also, the use of "or" means "and/or" unless stated otherwise. Similarly, "comprise," "comprises," "comprising" "include," "includes," and "including" are interchangeable and not intended to be limiting.

[0010] It is to be further understood that where descriptions of various embodiments use the term "comprising," those skilled in the art would understand that in some specific instances, an embodiment can be alternatively described using language "consisting essentially of" or "consisting of."

[0011] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which this disclosure belongs. Although methods and

materials similar or equivalent to those described herein can be used in the practice of the disclosed methods and compositions, the exemplary methods, devices and materials are described herein.

[0012] Any publications discussed above and throughout the text are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the inventors are not entitled to antedate such disclosure by virtue of prior disclosure.

[0013] In a study performed in 1977, heat treated human milk proteins were shown to degrade. For example, it was shown that immunoglobulins, lactoferrin, lysozyme, vitamin B12 and folate-binder proteins, and lactoperoxidase protein degraded. Holder pasteurization (62.5 °C 30 minutes) reduced the IgA titer by 20 percent, and destroyed the small content of IgM and most of the lactoferrin. Lysozyme was stable to this treatment, but with an increase in temperature there was progressive destruction, to near 100 percent at 100 °C. The same was broadly true of the capacity of milk to bind folic acid and protect it against bacterial uptake; with vitamin B12 the binder was more labile at 75 °C than at 100 °C (Ford JE *et al.* Influence of the heat treatment of human milk on some of its protective constituents. J Pediatr. 1977 Jan;90(1):29-35).

[0014] Preterm infants have poor or underdeveloped immune systems and immature digestive systems. Because of this, such preterm infants have increased total caloric and specific nutrient needs (when generally compared with term infants). Furthermore, it is well recognized the human milk contains not only the nutritional/caloric needs, but also provides important biological molecules for immune resistance and development. Thus, providing a proper balance of caloric

and biologically important materials is an important factor in their growth and development.

[0015] The disclosure provides human milk compositions and methods of making and using such compositions for feeding to infants, *e.g.*, premature infants. The compositions of the disclosure are derived from human milk and thus comprise human milk proteins; however, unlike pasteurization processes, the methods of preparing and the resulting compositions do not have the same degree of protein degradation/inactivation as typically found in pasteurized processes.

[0016] It is generally accepted that sterilized articles or devices purporting to be sterile attain a 10^{-6} microbial survivor probability, i.e., assurance of less than 1 chance in 1 million that viable bioburden microorganisms are present in the sterilized article or dosage form. With process stable articles, the approach often is to exceed the critical process parameters necessary to achieve the 10^{-6} microbial survivor probability (overkill) of any pre-sterilization bioburden. The sterility assurance of a sterilization process is attained through the use of a biological indicator; however its efficacy for any application is associated with the bioburden present during routine operation.

[0017] Success with sterilizing filtration has been predominantly accomplished over the last 30 years using 0.2µm filters. When coupled with appropriate process controls and integrity test methods there have been comparatively few incidents of contamination associated solely with the filtration process. In specialized settings, larger or smaller pore size filters may be appropriate.

[0018] Pasteurization processes merely reduce biological risks by heat treatment and are typically characterized as having a reduced bioburden for about 30 days. In contrast

the products and methods of the disclosure reduced biological contaminants (bacterial and viral) and in many instances can be considered "sterile" having a bioburden that does not result in any contamination or microbial degradation of nutrient or microbial growth for at least 60 days.

[0019] In one embodiment, the disclosure provides a sterile human milk protein lyophilized composition comprising about 4-5 mg of human milk protein per Decaliter when reconstituted in sterile water.

[0020] The disclosure provides lyophilized or reconstituted human milk protein compositions, *e.g.*, compositions that include human oligosaccharides, peptides, and other small molecules and methods of making and using such compositions. The compositions contain various levels of nutritional components and can be used in feeding of or administration to preterm and full term infants, as well as children and adults with various disorders and/or diseases. The compositions are generated by clarifying human skim milk followed by micron and submicron filtration, lyophilization and viral heat treatment. The resulting product comprises sterile human milk proteins in a lyophilized form. The lyophilized proteins can be reconstituted in sterile water or in a mother's milk before feeding to her baby. In one embodiment, the lyophilized product is reconstituted to provide about 3.5-5.0 grams of protein per decaliter (*e.g.*, 4.0-4.8, 4.2-4.6, 4.3-4.5 grams per decaliter).

[0021] In the methods of the disclosure, human milk is obtained, including pooled human milk. The human milk is then separated into cream and skim through various methods including gravitational separation or through centrifugation. The skim portion of the milk often includes large products that can clog a filter during filtration. Accordingly, the methods of the disclosure comprises a clarification process

to remove large particulars. Such methods can include passing the skim milk through diatomaceous earth or a large micron filter (e.g., about 5-10 microns). The clarification process may comprise one or more passages of the skim through a micron filter or diatomaceous earth (or a combination thereof). The resulting clarified skim can then be stored by freezing or immediately further sterile filter. The sterile filtration of the clarified skim can be performed through one or more filters having the same or graduated filter sizes. For example, in one embodiment, the clarified skim can be filtered through a 0.45 micron filter, followed by a second, 0.2 micron filter. In another embodiment, the clarified skim can be filtered through one or more 0.2 micro filters or one or more 0.45 micron filters or a combination thereof. The resulting sterile filtered skim milk has a reduced bioburden and can be bacterial free. The resulting sterile filtered skim milk can then be freed-dried or lyophilized to provide a lyophilized sterile milk protein composition. This lyophilized sterile milk composition can then be heat treated to eliminate viral contaminants providing a sterile human milk protein composition. The lyophilized product may be stored for 6 months or more without degradation or contamination so long as sterile processes are followed. Furthermore, the lyophilized composition can be readily reconstituted in sterile water or may be reconstituted in human milk (e.g., a mother's own milk) to increase the protein content of the mother's milk. It may be desireable to add the lyophilized product to bovine milk or a mixture of human and non-human milk formulations.

[0022] The methods featured herein can be used to process donor milk, e.g., about 50-1800 liters of raw human milk. The raw milk may be pre-screened for biological contaminants or the donors screened for various risk factors or

infections. Methods of screening a subject are very similar to those used for screening donors of blood for blood supplies. For example, a donor may be screened for substance abuse, viral infections (*e.g.*, HIV, hCMV, Hepatitis A, B, or C and the like). The donor may also be screened for bacterial infections. The donor may also be qualified based upon recent travel activities (*e.g.*, to certain foreign countries), sexual behavior, and drug use. In yet other embodiment, subjects may be screened for milk content (*e.g.*, fat or protein content). In some embodiments, it may be desirable to collect milk from subjects that express high protein, low fat milk.

[0023] By "whole milk" is meant milk from which no fat has been removed. By "skim milk" is meant milk from which at least 75% of fat has been removed.

[0024] The terms "premature", "preterm" and "low-birth-weight (LBW)" infants are used interchangeably and refer to infants born less than 37 weeks gestational age and/or with birth weights less than 2500 gm.

[0025] The term "full term" infant is used to refer to infants born after 37 weeks gestational age and/or with birth weights greater than 2500 gm.

[0026] By "bioburden" is meant microbiological contaminants and pathogens (generally living) that can be present in milk, *e.g.*, viruses, bacteria, mold, fungus and the like.

[0027] Fig. 1 shows one embodiment of a method of obtaining human milk protein. As discussed above, donor milk can be carefully analyzed for both identification purposes and to avoid contamination. The donor milk may be frozen or unfrozen, pooled or unpooled. If the donor milk is frozen, the donor milk is thawed. The thawed donor milk may be pooled following thawing or may be pooled prior to freezing.

The raw milk is then separated into skim and cream. The separation of the skim from the cream may be performed by any number of methods known in the art including, but not limited to, gravitational separation or by centrifugation. Because directly applying the skim to sterile filters will cause rapid clogging of the filter system, the skim milk is first clarified before sterile filtration. The clarification of the skim may be performed by passing the skim through diatomaceous earth or through large pore filters (*e.g.*, from 5 micron to 50 micron filters). In some embodiment, the clarification step may comprise a combination of filters or filters and diatomaceous earth. For example, a first clarification filter may comprise a 45 micron filter followed by a 20 micron and a 5 micron filter. It will be recognized that any filter size in between and inclusive of 5 and 50 microns can be used.

[0028] The permeate from the clarification step is then processed through one or more sterile filters. The sterile filters are about 0.2 microns to 0.45 microns. In some embodiment, the permeate from the clarification step is filtered through one or more graduated sterile filters (*e.g.*, a 0.45 micron filter and then a 0.2 micron filter). The permeate from the sterile filtration can then be combined with other permeates from different sterile filtrations batches. The resulting permeates are freeze-dried/lyophilized to provide a dry human milk protein composition. The lyophilized/freeze-dried composition can then be further sterilized by a viral heat activation step or by gamma irradiation or other techniques known in the art.

[0029] The resulting lyophilized/freeze-dried product can be easily stored in sterile containers for at least 6 months or more. The lyophilized/freeze-dried product can be reconstituted in bovine milk, human milk (*e.g.*, milk from the

mother of the baby to be fed), or sterile solutions (*e.g.*, water). The reconstituting fluid can be further supplemented with vitamins, minerals, oligosaccharides, fatty acids and other nutritional factors. In one embodiment, the lyophilized product is reconstituted to a final concentration of about 4.0-5.0 mg/DL of protein. In another embodiment, the reconstituted milk protein is fed to a neonate from 2-8 times per day or as necessary or desired.

[0030] For example, human breast milk was centrifuged at 10,000 x g for 30 minutes and passed through 25 µm filter paper to remove large particles. 1200 mL were passed through a Sartoclean GF 3 + 0.8 µm filter (Sartorius 5605304E7--SS) which reached a final pressure 12.0 psi. The entire 1200 mL were then passed through a Sartoclean GF 0.8 + 0.65 µm filter (Sartorius 5605305G7--SS) without any backpressure. Of the 1100 mL of filtrate remaining, 800 mL were passed through a Sartoclean CA 0.45 µm filter (Sartorius 5625306A7--SS). The entire 800 mL of remaining filtrate were passed through a Sartoclean 0.2 µm filter (Sartorius 5625307A7--SS) without any detectable pressure. In other embodiments, the filters can be ceramic filters.

[0031] Figure 2A-C depicts general schematics of systems of the disclosure for obtaining human milk protein in a sterile composition.

[0032] The disclosure also provides kits comprising a lyophilized/freeze-dried human milk protein composition in a vial or other storage container; a syringe or other container for holding a reconstituting liquid. The vials and liquid containers may be in a unit dose form. The reconstituting liquid may comprise additional nutritional factors or therapeutics.

[0033] The following examples are meant to exemplify but not limited the disclosure.

EXAMPLES

[0034] Two samples of frozen human milk were provided for filterability studies to optimize a filter train suitable for filtering a 200 L batch with a 25% overcapacity to anticipate product and process variations. The first 3 liter sample was decanted for 24 hours to reduce the fat content and the second 15 L sample was decanted for 36 hours. Samples were kept frozen at -15°C to -20°C until thawed.

[0035] Eleven filtration runs were made utilizing two different filters in the first position, four combinations in the second position and three different sterilizing-grade 0.2 µm filters. The first one liter containing of the 24 hour milk thawed for approximately 42 hours in the refrigerator before it was transferred to a room temperature rotator for the final thaw. On the same day, a second liter of milk was thawed in approximately 45 minutes in a 37 °C water bath after rotating for almost 3 hours at room temperature. The fast thawed material was significantly easier to filter at the submicron level than the slowly thawed material. Subsequent containers of milk were thawed as quickly as possible using a 37 °C water bath or a rotator in a 37 °C incubator. The water bath has better heat transfer properties than the incubator and thus the milk thawed faster. A variation that can be used would include a shaker water bath. Care should be taken to mix the thawing milk to equilibrate the temperatures and prevent overheating of the milk. The milk was refrigerated after thawing before it was processed any further.

[0036] In the first clarifying filter position, it was determined that a 5 micron DeltaMax™ DMG4 polypropylene depth filter protected the Protec® filter better than the 10 micron ALpHA® MF10.

[0037] DeltaMax™ filter were not available I disc format and the 36 hours decanted milk was used to size the filter using a small capsule (CSDMG5-772). The chilled milk was stirred while being filtered. Almost 15 L were filtered in a total of 66 minutes using a pup set at 260 mL/min. The filter did not plug. Separated fat and clumps of milk precipitate collected inside the capsule. Pressure increased from 0 to 6 psi. A 235 L batch could be easily filtered at 3 LPM using a 30" DeltaMax™ DMG5 filter.

[0038] In the second clarifying filter position the Protec® RF0.5 glass microfiber filter was used. Rapidly thawed 24 hour and 36 hour decanted milk pre-filtered by the DMG5 was readily filtered at 10 psi. Twice as much throughput was possible with the 24 hour decanted milk versus the 36 hour decanted milk. A 30" RF0.5 filter is capable of filtering up to 5400 L of 24 hour milk, provides for variation in milk quality and permits filtration at 3 LPM matching the DeltaMax™ prefilter. It should be noted that attempting to flow faster than 1 LPM/10" RF0.5 would result in rapid premature plugging of the filter.

[0039] A filtration scheme that uses a pump set at 3 LPM and tubing system capable of producing up to 20 psi upstream pressure is able to filter the 200 L batch through the 30" DeltaMax™ DMG5 and the 30" Protec® RF0.5 if the milk is thawed quickly. This allows up to 5 psi differential pressure for the first filter and 10 psi differential pressure for the second filter with 5 psi pressure to spare. The milk can be collected in a bag or other sterile collection divide for transport to a sterile filtration area. Typically all the filtration will take place in a cold room or in a manner such that the milk is chilled before and after filtration.

[0040] The final sterile filtration uses about seven 30" EverLUX™ STW0.2 filters for the 200 L batch and the addition of addition filters should be considered for larger batches (e.g., eight (233 L) or nine (272L) etc.). Each 10" STW0.2 filter module can filter approximately 9.7 L. With nine cartridges in a single housing, a flow rate of ~1.9 LPM may be possible at 10 psi. Seven cartridges allow ~1.5 LPM. A separate pump or pressure source should be used for the final filtration.

[0041] If disposable capsules are used, the total flow rate is divided amongst all the capsules. That is, for 9 capsules, each capsule will have a flow rate of about 200 ml/min.

[0042] Two runs were made using diatomaceous earth (DE) materials for the clarification step followed by filtration through 0.2 micron filters. Table 1 below demonstrates the resulting data.

[0043] Table 1:

Sample	Lactoferrin (µg/ml)	Lysozyme (µg/ml)	IgA (mg/ml)	Protein (mg/ml)
Control (DE raw skim)	1.51	14.35	0.355	not meas'd.
Control (DE raw skim)	1.71	13.91	0.356	not meas'd.
Average	**1.61**	**14.13**	**0.355**	not meas'd.
Filtered with STW0.2(1)	1.29	9.49	0.179	
	1.14	7.82	0.172	
	1.51	8.83	0.184	
	1.48	8.18	0.161	
	1.48	8.74	0.196	
Average	**1.40**	**8.61**	**0.18**	

[0044] Table 1 demonstrates that the filtration provides a sterile composition comprising at least 45% or more of the initial starting human milk proteins listed above.

[0045] Other variations and embodiments of the invention described herein will now be apparent to those of ordinary skill in the art without departing from the scope of the invention or the spirit of the claims below.

WHAT IS CLAIMED IS:

1. A method comprising:

sterile filtering skim human milk through at least two successively smaller submicron filters to obtain a human milk protein composition;

lyophilizing the human milk protein composition; and

applying a viral inactivation step and/or a sterilizing process to the lyophilized human milk protein composition.

2. The method of claim 1, wherein the skim human milk is obtained by gravity separation for 24-36 hours or by centrifugal separation.

3. The method of claim 1, wherein the skim human milk is clarified prior to filtration through at least one clarifying filter.

4. The method of claim 3, wherein at least one of the clarifying filters comprises a micron filter or diatomaceous earth.

5. The method of claim 4, wherein the at least one clarifying filters comprises two clarifying filters.

6. The method of claim 5, wherein a second clarifying filter is a submicron filter.

7. The method of claim 1, wherein the at least two submicron filters are between about 0.5 and 0.2 micron filters.

8. The method of claim 1, wherein the viral sterilizing step comprises heat treatment.

9. The method of claim 1, wherein the viral sterilizing step comprises gamma irradiation.

10. The method of claim 1, wherein the lyophilized product comprises proteins that upon reconstitution in a liquid are biological active.

11. The method of claim 10, wherein the lyophilized product comprises at least 50% of the skim milk's lysozyme content.

12. The method of claim 10, wherein the lyophilized product comprises at least 40% of the skim milk's IgA content.

13. The method of claim 10, wherein the lyophilized product comprises at least 80% of the skim milk's lactoferrin content.

14. The method of claim 1, wherein the lyophilized human milk product comprises a storage life of about 1 year or more.

15. The method of claim 1, wherein following the sterile filtration the skim human milk comprises about 20-50 mg/ml protein.

16. The method of claim 15, wherein the skim human milk comprises about 1900-2400 µg/ml lactoferrin, about 12-18 µg/ml lysozyme and/or about 1-3 mg/ml human IgA.

17. The method of claim 1, wherein the human skim milk is non-pasteurized.

18. A lyophilized human milk product obtained by the process of claim 1.

19. A sterile lyophilized human milk product obtained from non-pasteurized human milk comprising human IgA, human lactoferrin, and human lysozyme proteins.

20. A lyophilized human milk protein composition wherein wen reconstituted in comprising about 4.2 g/DL protein when reconstituted in a non-protein containing medium.

21. A human milk composition prepared by mixing the lyophilized human milk product of claim 18 with milk from a mother of an infant to be fed.

22. A method of treating a neonatal subject comprising feeding the subject the milk product of claim 19, 20 or 21.

23. The method of claim 22, wherein the feeding comprises about 0.5 grams protein per feeding unit.

24. The method of claim 22, wherein the feeding is given about 8 times per day.

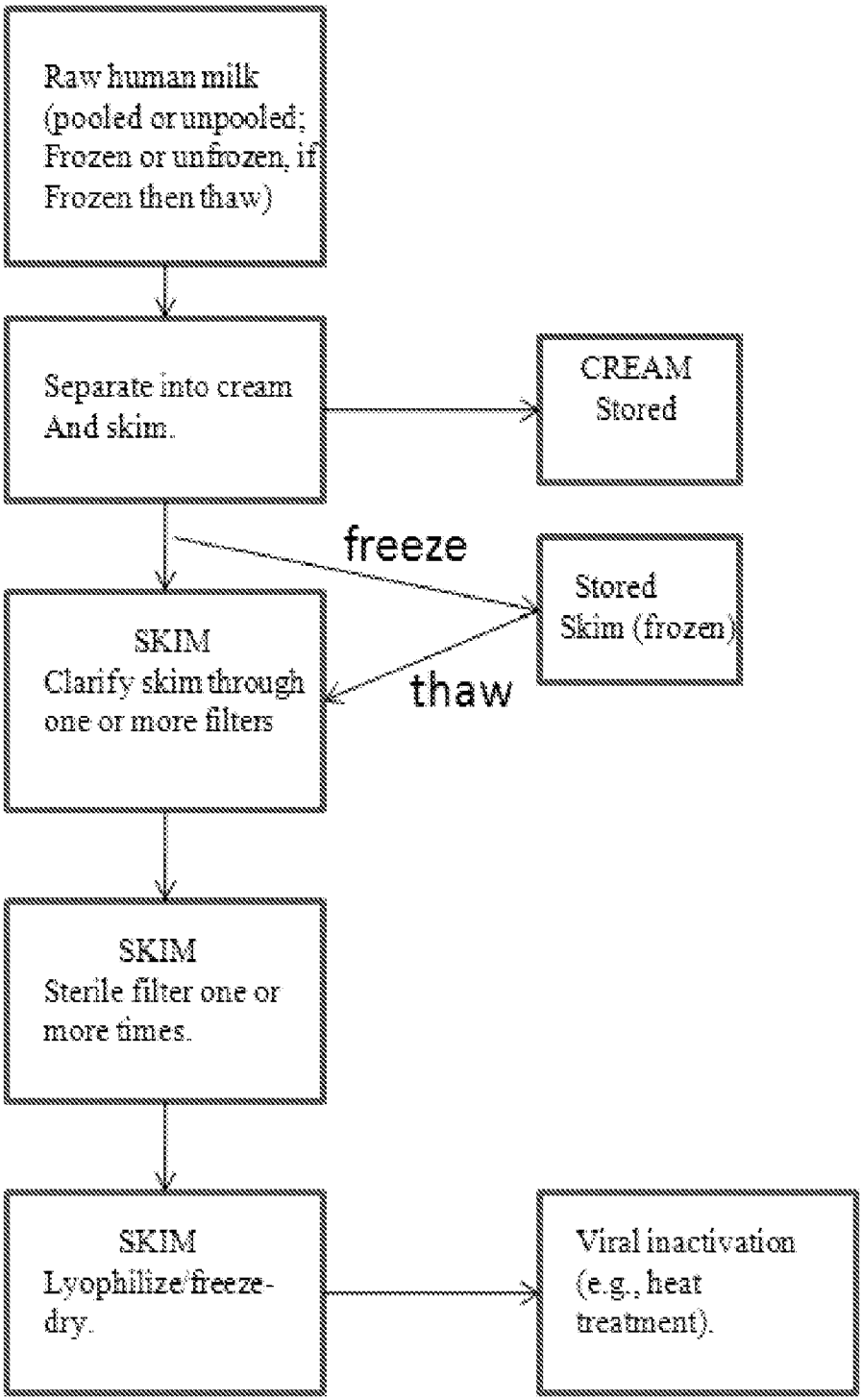
Raw human milk (pooled or unpooled; Frozen or unfrozen, if Frozen then thaw)
Separate into cream And skim.
CREAM Stored
freeze
Stored Skim (frozen)
thaw
SKIM Clarify skim through one or more filters
SKIM Sterile filter one or more times.
SKIM Lyophilize/freeze-dry.
Viral inactivation (e.g., heat treatment).

FIGURE 1

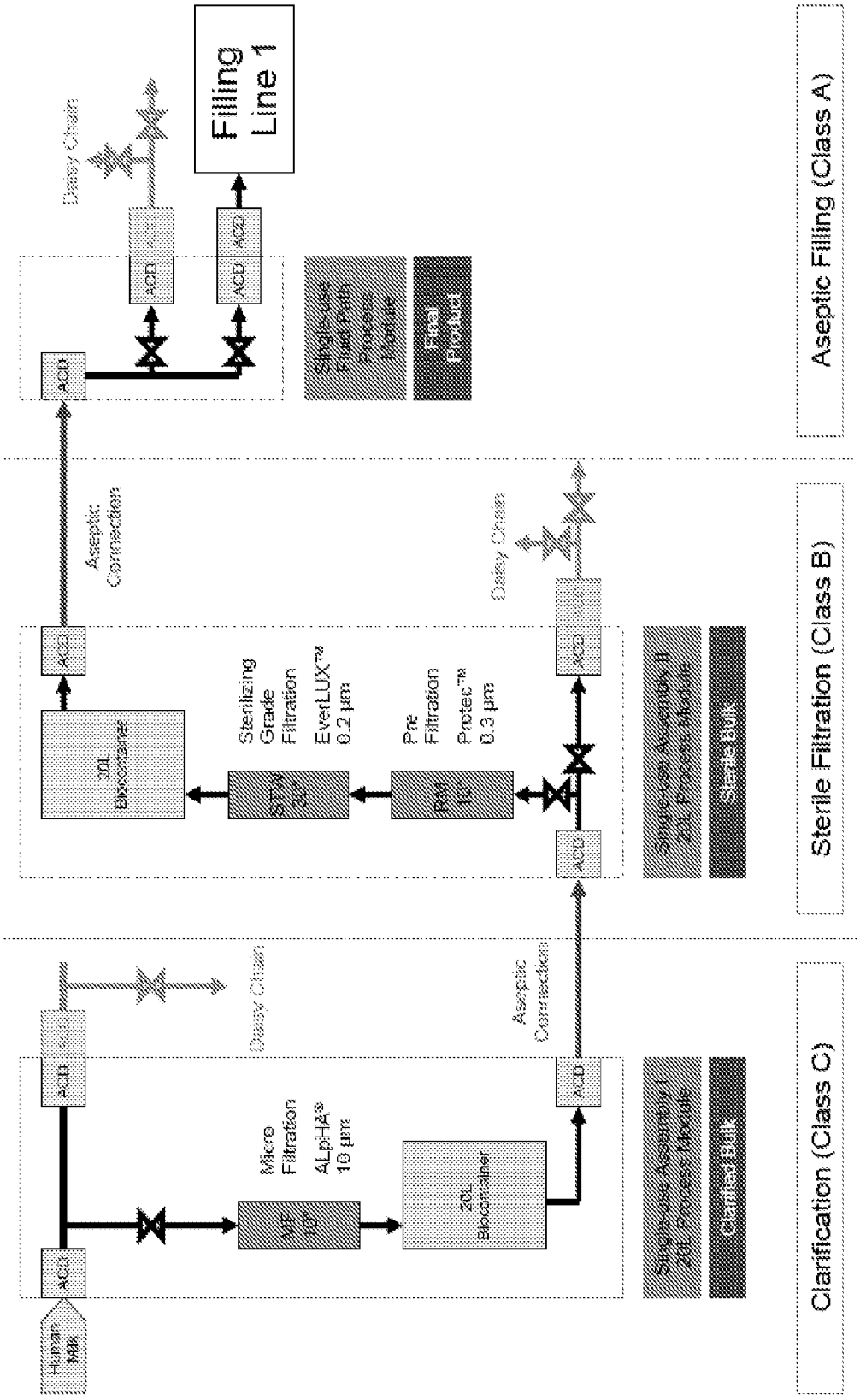
Clarification (Class C)
Sterile Filtration (Class B)
Aseptic Filling (Class A)
Human Milk
ACD
Micro Filtration 4LpHA® 10 µm
20L Bioreactor
Single-use Assembly I 20L Process Module
Clarified Bulk
Aseptic Connection
Sterilizing Grade Filtration EverLUX™ 0.2 µm
Pre Filtration Protec™ 0.3 µm
Single-use Assembly II 20L Process Module
Sterile Bulk
Single-use Fluid Path Process Module
Filling Line 1
Final Product

FIGURE 2A

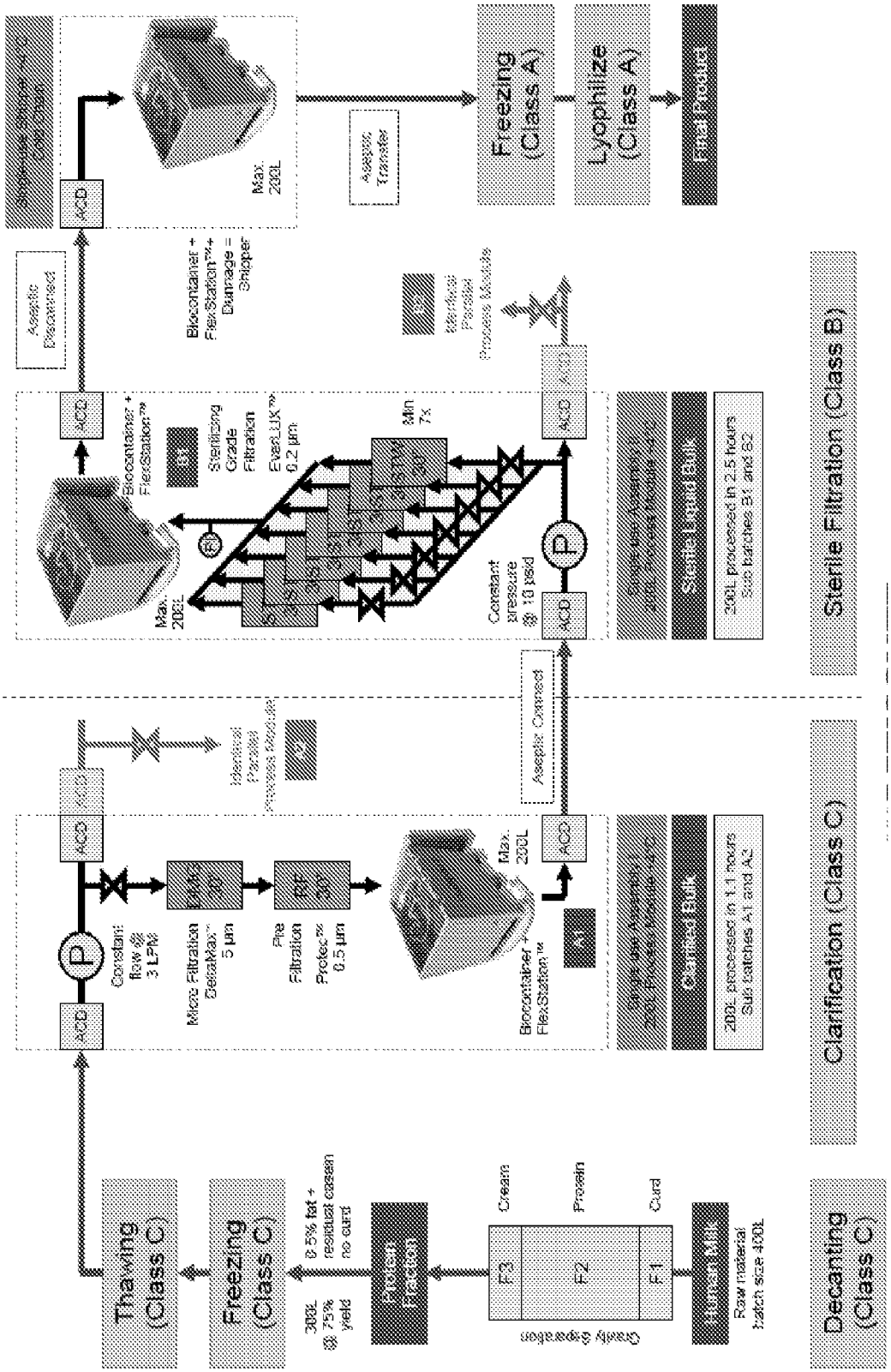
Thawing (Class C)
Freezing (Class C)
8.5% fat + residual casein no curd
75% yield
Protein Fraction
Cream
Protein
Curd
F3
F2
F1
Whey separation
Raw material batch size 400L
Decanting (Class C)
Clarification (Class C)
Constant flow @ 3 LPM
Micro Filtration BetaMax™ 5 µm
Pre Filtration Protect™ 0.5 µm
Max. 20L
Biocontainer + FlexStation™
Aseptic Connect
Constant pressure @ 10 psid
Min 7x
Sterilizing Grade Filtration EverLUX™ 0.2 µm
Biocontainer + FlexStation™ + Drainage = Shipper
Aseptic Disconnect
Aseptic Transfer
Freezing (Class A)
Lyophilize (Class A)
Final Product
Sterile Filtration (Class B)
Clarified Bulk
Sterile Bulk
200L processed in 1.1 hours Sub batches A1 and A2
200L processed in 2.5 hours Sub batches B1 and B2

FIGURE 2B

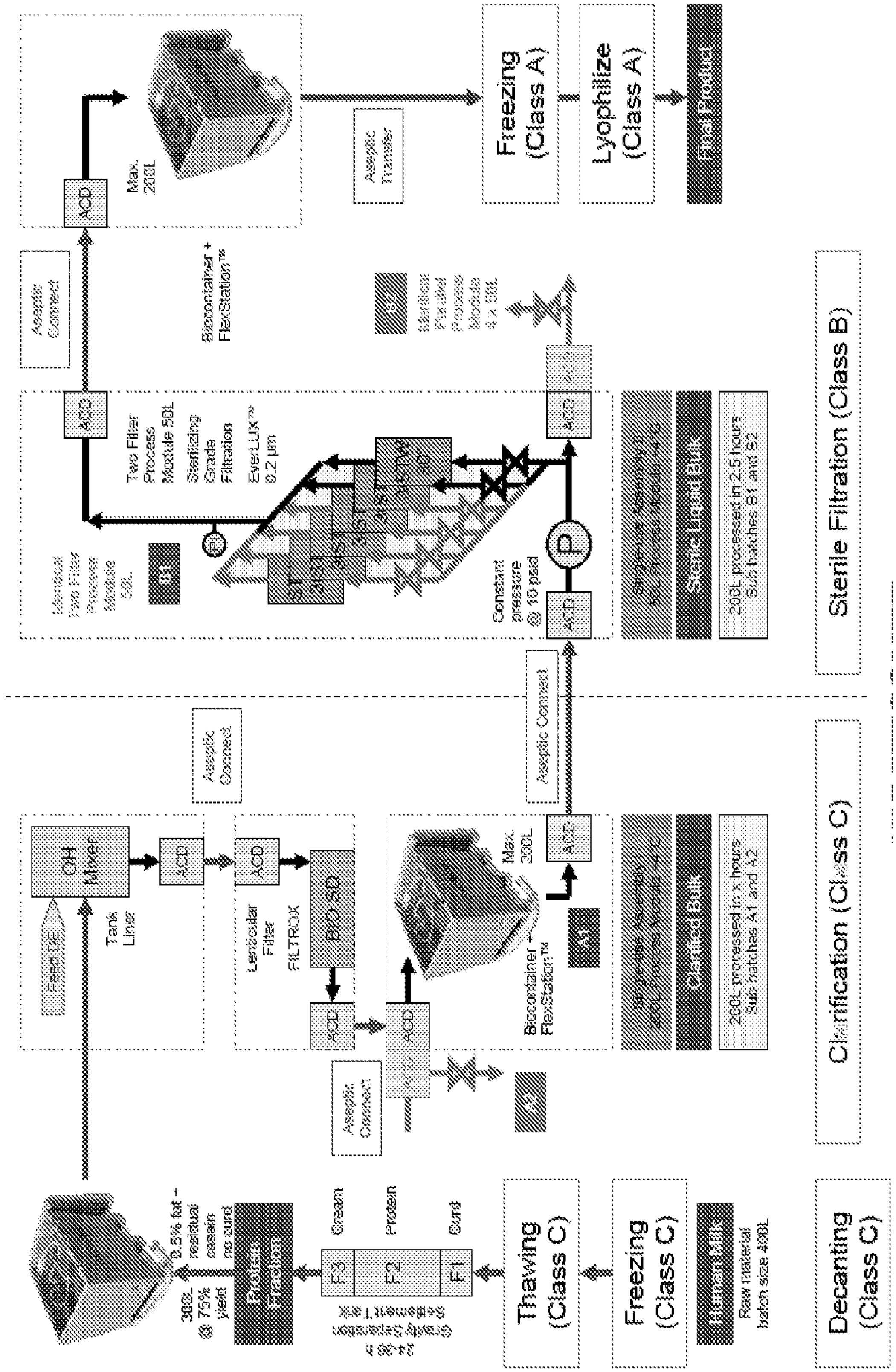
Freezing (Class A)
Lyophilize (Class A)
Final Product
Aseptic Transfer
Aseptic Connect
Bioconatiner + FlexStation™
Max. 200L
ACD
Two Filter Process Module 50L
Sterilizing Grade Filtration
EverLUX™ 0.2 µm
B1
B2
Constant pressure @ 10 psid
P
Sterile Liquid Bulk
200L processed in 2.5 hours Sub batches B1 and B2
Sterile Filtration (Class B)
OH Mixer
Feed DE
Tank Liner
Lenticular Filter
FILTROX
BIO SD
A1
A2
Clarified Bulk
Clarification (Class C)
Cream
Protein
Curd
F3
F2
F1
Protein Fraction
0.5% fat + residual casein no curd
Thawing (Class C)
Freezing (Class C)
Human Milk
Raw material batch size 400L
Decanting (Class C)

FIGURE 2C