From:	Drummond Food Science Advisory
To:	Morissette, Rachel
Subject:	Re: Questions for GRAS Notice No. GRN 000669
Date:	Wednesday, November 23, 2016 7:34:33 AM
Attachments:	Amended Pages.zip Appendix Pages Updates.zip GRN 669 FDA Response to Letter of 8 Nov _ 23 Nov 2016.pdf
Importance:	High

Dear Rachel

Please find attached a letter of response to the questions raised in your letter of 8 November 2016.

Clean copies of specific sections have been provided as separate documents as it was rather cumbersome and awkward as a single document, however I appreciate this may not work for your purpose so would appreciate any further suggestions.

As you will note one of the key areas of Confidentiality has been addressed. Discussions with Synlait regarding the importance of transparency and availability of information have met with a positive response and significant changes to the status of much of the information in Part 7. I do hope this is useful.

With kind regards

Lynley

On 19/11/2016, at 1:34 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:

Lynley Drummond
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Dear Lynley,

A revised copy of the entire notice is not required and not preferable. Please provide point-by-point responses in a separate document, which will serve as an amendment to the original notice. A clean copy of specific sections of the notice can be provided in the same document as the point-by-point responses. The original version of the notice is the one that appears on the FDA GRAS notice website, with the amendment available for request through FOIA. Hope this helps. Please let me know if you have further questions.

Best regards,

Rachel

Rachel Morissette, Ph.D.
Consumer Safety Officer
U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Biotechnology and GRAS Notice Review
5001 Campus Drive, HFS-255
College Park, MD 20740-3835
Email: Rachel.Morissette@fda.hhs.gov

From: Drummond Food Science Advisory [mailto:lynley_dfsa@me.com]
Sent: Thursday, November 17, 2016 9:11 PM
To: Morissette, Rachel
Subject: Re: Questions for GRAS Notice No. GRN 000669

Dear Rachel

As we are working through the reply to the questions raised in your letter of 08 Nov, I just wanted to check in with you regarding the structure of the reply. As some amendments to the Notice itself are required, the intent is to provide an updated version of the Notice, accompanied by a letter of explanation / guidance around the specific changes.
I would really appreciate your comment as to whether this is an acceptable way to resolve some of the points, or if this is not a preferred option, what would be.

With sincere thanks in advance

Best regards
Lynley

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On 10/11/2016, at 2:43 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:

Thanks!

Rachel

Rachel Morissette, Ph.D.
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Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Biotechnology and GRAS Notice Review
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Email: Rachel.Morissette@fda.hhs.gov

From: Drummond Food Science Advisory [mailto:lynley_dfsa@me.com]
Sent: Tuesday, November 08, 2016 4:55 PM
To: Morissette, Rachel
Subject: Re: Questions for GRAS Notice No. GRN 000669

Dear Rachel

Thank you for the questions raised, I acknowledge receipt and the 10

working day response time.

With sincere thanks
Lynley

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On 9/11/2016, at 7:57 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:

<11-8-16 GRN669 Questions for Notifier.pdf>

Drummond
Food Science Advisory Ltd

Dr. Rachel Morissette, Ph.D.
Consumer Safety Officer
U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety (OFAS)
Division of Biotechnology and GRAS Notice Review

23 November 2016

Dear Dr. Morissette

Thank you for your letter of November 8 2016 outlining a number of questions raised during the review of GRN 000669. Please find below the responses to those questions – numbered specifically as per your original letter. In addition, the responses necessitated a number of minor amendments to specific parts of the original Notice submitted. To that end this letter is accompanied by a number of attachments that are identified as to their position in the Notice, by their file title.

1. Clarification of intended use of bLF:
    a. The intended use of bLf subject to this notice includes ALL forms of infant formula (powder, ready-to-feed, and liquid concentrates). The addition rate to the potential range of formula formats is on a per solids basis (up to 100 mg/ 100g of formula solids).
    b. The intended use of bLf is limited to non-exempt milk-based term infant formulas. The statement of "exempt" on page 6 is in error and should read "non-exempt". A copy of corrected page 6 is provided with this response
2. Specifications:
    a. Lactoferrin detection is by ultraviolet-visible(UV-vis) spectrometry recording at 220 nm. Lactoferrin separation is achieved by reverse-phase high performance liquid chromatography (RP-HPLC). Table 2-5 (page 34) has been amended to include the detection methods, and a copy is provided with this response.
    Testing is conducted at NZ Government owned laboratories called AsureQuality, who operate ISO 17025-accredited facilities across New Zealand. These laboratories are accredited by International Accreditation New Zealand (IANZ), a signatory to the International Laboratory Accreditation Cooperation's Mutual Recognition Arrangement (ILAC MRA).
    For the analysis of "Lactoferrin Purity", AsureQuality employ a proprietary method developed and validated by Callaghan Innovation for Synlait, as presented in Part 7: Appendix 3 pages (A3:2-A3:9). Synlait acknowledges the need for this method to be public, and as such has amended the status to being

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non-confidential and generally available. An amended cover page for Part 7: Appendix 3 is provided with this response.

b. Residual fat in bLf. Fat removal is related to processing capability, as opposed to safety considerations for bLf. The lactoferrin plant and process equipment are not designed to handle high levels of fat and therefore a standard skim milk stream, containing the lactoferrin component is utilised for separation of the bLf.

   The process for fat separation is a standard process in any dairy factory and uses a milk centrifugal separator which operates to separate the skim and cream based on different densities. Levels of fat in the skim and cream streams are monitored regularly throughout processing to ensure adequate skimming efficiency is attained. Hence the limit for fat as a raw material control factor is contained in the Raw Material specification in Appendix 1 A1:16, for the raw material (skim milk) stream that enters the lactoferrin plant.

c. The "Error" link on page 31, should have read "Table 2-9". This has been corrected and a copy of the corrected page 31 is provided with this response.

d. Aluminium levels in the bLf Specification. Table 2-7 has been amended to include analytical results for aluminium, and the status of the Synlait Lactoferrin Specification in Part 7: Appendix 1 (pages A1:2-A1:5) has been updated to non-confidential. An amended copy of Table 2-7 is provided with this response.

e. Corrections:

   i. The specification limits for the minimum protein content and lactoferrin content as a % of protein in Table 2-7 have been corrected. An amended copy of Table 2-7 is provided with this response.
   ii. Solubility measurement. The solubility of lactoferrin is assessed by preparation of a 2% solution at 20°C and two (2) methods of determination. The first is a transmittance measurement at 600 nm against a distilled water blank. This provides a quantitative measure % transmittance (80-100%). The second is a word such as Complete, or Transparent, which is used to describe compliance to a transmittance level of 80-100%. The 2 reporting methods are recorded to meet the requirements of various regulatory specifications (Table 2-6 page 36-37) and provide comparative information to the specifications of other manufacturers. The temperature of the test solution has been included in the updated version of Table 2-7, provided with this response.
   iii. Coliform and *E.coli* test methods.
   The microbiological methodology used to quantify coliforms and detect *E. coli* is specified under the same published method (ISO 11866-1/IDF 170-1). The correct methodology information has been updated in Table

2-5 (page 34 -35) and results for the batches of lactoferrin in Table 2-7 added (page 38-39). Copies of each of these updated tables are provided with this response. In addition, the detection method for these organisms in the Synlait specification provided in Part 7: Appendix 1 (page A1:3) has been corrected and the updated page accompanies this response.

Table 2-6 (page 36-37) and Table 2-8 (page 40-41) only include information for Coliforms as these tables provide comparative information for lactoferrin specifications across various regulatory jurisdictions and compare data that is common and available between manufacturers. There is no complete comparative data for all companies so only that which is complete has been detailed.

iv. Foreign Matter and Sediment are two distinct tests and the test methodology for each is listed in the specification in Part 7: Appendix 1 (A1:3 – A1:5). These are standard international dairy product tests and sediment (ADMI Bull. 916 1990) does include scorched particles based on the standard chart included in this method (i.e. category A is ≤7.5mg, excluding extraneous matter, retained on the filter pad). For Foreign Matter according to AS 2300.4.5 – 1994, this is defined as "extraneous matter – examine the filter disc for extraneous matter (e.g. hair, wood, metal, dust and insect fragments) by visual inspection and record accordingly."

Table 2-5 and table 2-7 have been updated to reflect this prior omission and are provided with this response.

3. Compliance of Milk with U.S. regulations:
    a. The fluid milk starting material is produced in compliance with good agricultural practices for dairy farming. All farms supplying milk to Synlait are required to be compliant with a Government Code of Practice for dairy farms(NZCP1). Compliance to this standard requires an independent third party audit process to be in place for each farm to verify compliance with NZCP1.
    b. The fluid milk starting material is produced in compliance with applicable U.S. regulations, including meeting tolerances for veterinary drugs (21 CFR Part 556), polychlorinated biphenyls (PCBs) (21 CFR 109.30 for PCB's), and pesticides in milk and/or milk products (40 CFR Part 180). The pasture based system of farming in New Zealand results in a comparatively low use of pesticides, which along with veterinary medicines, all require registration with the Ministry for Primary Industries (MPI), Agricultural and Veterinary Medicines (AVCM) Group. All registrations of pesticides and veterinary medicines and usage, must be maintained and made available for audit by independent third party as approved by MPI.

    The use of PCB's was prohibited from farm dairies by the NZ Dairy Board in the 1980's, and requirements since then have ensured they are not in use.

    Verification of compliance to applicable U.S. regulations for veterinary drugs,

polychlorinated biphenyls (PCBs), and pesticides in milk is conducted via the National Chemical Contaminants Programme (NCCP), which involves testing of several hundred Synlait raw milk samples taken every year by MPI approved verification agencies. Since the registration and implementation of their RMP, Synlait has complied with this random sampling and testing programme. We have not received notification of any non-compliant test results from these samples.

c. Pesticide and veterinary drug levels in fluid milk starting material do not exceed FDA action levels for pesticides as listed in CPG 575.100 or safe levels for veterinary drugs, in accordance with Appendix N of the Grade "A" Pasteurized Milk Ordinance (PMO, 2015), M-I-05-5, issued Sept. 27, 2005). All Veterinary Medicines available in NZ for use on dairy farms must be approved under the Agricultural and Veterinary Medicines (ACVM) Act 1997, which is administered by the ACVM Group within MPI. One of the key aspects the ACVM look at when registering products is "risk to trade", meaning that a review of relevant legislation for key trading partners plays a key part in controlling registered medicines. Under this regime we can be confident that the veterinary medicines available in NZ will be in compliance with the relevant US standards when used as per label. Under the Act, veterinary medicines are only available via veterinarians, and vets have a number of responsibilities under the Act to ensure appropriate use of these chemicals, including the exclusion of animals from milking until after any prescribed withholding period has been completed. Compliance with these requirements at individual farm level is verified annually by an independent third party audit, as discussed in 3a above.

d. The monitoring of levels of Radionuclides in milk produced in New Zealand is covered under the NCCP testing programme listed in 3b above. There have been very low levels of radioactive contamination detected in milk due to the geographic isolation of New Zealand, and that New Zealand is a "nuclear free" country. The detected levels are well below the derived intervention levels (DIL's) noted in CPG 560.750 in Bq/kg. This is not part of the quality control specifications for raw milk. There is a history of very low levels of radionuclides in raw milk in New Zealand and this continues to be monitored through raw milk testing programmes and the testing of dried milk products for levels of radionuclides on a regular basis.

e. HACCP program. The confidentiality of the certification of the Synlait HACCP program (Part 7: Appendix 2 page A2:3) has been changed to non-confidential. Synlait considers that this plan concurs with that outlined in the Grade "A" PMO (2015). In addition, a copy of the Codex Alimentarius HACCP System and Guidelines (CAC/RCP 1- 1969 Rev. 4- 2003, Annex) has been provided for reference with this response.

4. Method of Manufacture:

   a. Synlait advises that all filtration media and processing aids used in the manufacture of Synlait lactoferrin are used in accordance with the food contact regulations and are authorized in the U.S. for use in contact with milk.
   b. The food contact notification (FCN) for the Sepharose Big Beads used for the separation of lactoferrin form milk (SP Sepharose Big Beads) is confirmed as FCN 443 (CAS Reg. No 676618-71-6). In support of this an additional data sheet published by GE Healthcare is provided with this response (Sepharose Big Beads SP Data Sheet.pdf) confirming both the FCN and CAS Reg. No. SP Sepharose Big Beads resin is the permitted resin material for the removal of lactoferrin from milk in Australia and New Zealand according to the Australia New Zealand Food Standards Code – Schedule 18 – Processing aids.

Sulphonate agarose ion exchange resin	Production of lactoferrin from bovine milk and milk-related products	GMP

   FCN 531 proposed as the alternate citation in your letter of November 8, refers to "Q Sepharose Big Beads" (CAS reg. No 846853-13-2) which are also used for protein separation, but more commonly in applications such as the removal of protein from beer. In Australia and New Zealand, the agarose resin of FCN 531 is the permitted processing aid for the removal of protein and polyphenolic compounds from beer (Australia New Zealand Food Standards Code – Schedule 18 – Processing aids.

Substance	***Technological purpose***	***Maximum permitted and food level (mg/kg)***
Amine agarose ion exchange resin	Removal of specific proteins and polyphenols from beer	GMP

   c. Clarification step is where the skim milk is passed through a clarifier to remove any particulate matter, via centrifugal separation, prior to being pre-filtered through the 1 µm filter (Appendix 1 A1:6) to remove any further fine insoluble material and reduce the microbial load. Clarification is undertaken to ensure protection of the delicate processing equipment and materials further on in the process, from potentially damaging insoluble particles.
   d. Food Contact materials:

   Note the status of materials specifications in Appendix 1 has been changed to "non-confidential".

      i. All filtration membranes used in the manufacture of Synlait lactoferrin comply with permitted food contact regulations in the U.S. Filtration media product lines are manufactured using FDA complaint materials under the Food, Drug & Cosmetic Act under regulations (Part 7 Appendix 1 page A1:6 – A1:8)

21 CFR 177.1520 (c) 1.1
21 CFR 177.2800
21 CFR 178.3400

ii. SP Sepharose Big Beads comply with FCN 443

iii. The packaging material (Part 7: Appendix 1page A1: 27 – A1:19) consisting of coated polyester (14 µm) / ink / adhesive / foil (7 µm) / polyethylene (90 µm) is compliant under the Food, Drug & Cosmetic Act under regulation 21 CFR 177.1520 (c) 2.2 as the polyethylene is the food contact surface of the packaging material.

e. Salt specification:

i. The salt (RMIN00049) used as a processing aid in the manufacture of Synlait lactoferrin (Part 7: Appendix1 pages A1:9 – A1:15) complies with the relevant USP (USP 38/NF33 – 2015) and FCC (FCC 10 – 2016) monograph requirements for Sodium Chloride with respect to Ferrocyanide levels. The levels of Ferrocyanide are tested by the salt manufacturer for each lot of salt and are, without exception, consistently in the range of 3-6 mg/kg, which is well within the limits as listed in the FCC and USP monographs for this ingredient.

ii. The statement in Appendix 1 A1:9- A1:15 Synlait Specification RMIN00049 that the cheese salt (NaCl) ingredient is not allowed for use in Infant Formula is a comment added by Synlait in this specification to be clear that this ingredient is not for direct use in Infant Formula products which are also formulated and manufactured on site. The reason being, that Sodium Chloride, meeting FCC or USP Standards, is a permitted form of sodium for addition to infant formula under most in-market regulations (e.g. FDA, FSANZ, EU, CODEX) and therefore could possibly be added in product formulations.

iii. There are some significant differences between the processing steps involved for the manufacture of infant formula and lactoferrin. In the lactoferrin process, there are operations where the salt solution, including food additives, are physically separated from the lactoferrin solution by the use of membrane filtration technologies based on molecular weight differences. This is significantly different to the Infant Formula manufacture process, where levels of such a component would be effectively concentrated due to water removal.

iv. In ferrocyanide, cyanide ligands are bound strongly to the iron atom with an affinity of 10^{-35}M. To break the iron-cyanide complex requires strong acidic conditions (it is stable in stomach pH 1). Due to the high availability of sodium ions in the 1M NaCl solution used for elution and with only a very small amount (3-6 mg/kg) of sodium ferrocyanide it is extremely unlikely that the ferrocyanide complex would break to release ferrocyanides as sodium has a very high affinity for ferrocyanide.

v. After the elution step, the salt solution containing lactoferrin passes through a membrane filtration process with 30kDA pore size. The size of

the sodium ferrocyanide complex is 300 Dalton (100 times smaller than the size of ultrafiltration/diafiltration (UF/DF) membrane cut off). As such, the sodium ferrocyanide will easily pass through the UF membrane, with the majority removed during the UF step, while the lactoferrin is retained by the membrane. Further diafiltration of the lactoferrin with reverse osmosis (RO) water through 30kDa membranes is designed to remove any residual salt and sodium ferrocyanide molecules.

vi. Synlait has carefully considered the potential of breakdown and interaction of ferrocyanide during manufacture. In chemical terms, the potential breakdown of ferrocyanide and interaction with lactoferrin will almost certainly not occur under the conditions of lactoferrin manufacture.

vii. Cyanide ligands are bound strongly to the iron atom with an affinity of 10^{-35} M and to break the iron-cyanide complex it requires strong acidic conditions. Similarly, Lf binds to ferric iron (Fe+3) with high affinity (10-20M) and requires strong acid conditions (pH <2) to break the Lf-Iron complex. Even under these most unlikely conditions released cyanides will still be removed during the ultrafiltration and diafiltration (30 kDa) steps as outlined above, as these molecules will be a factor of over 100x smaller than the membrane pore size.

viii. Under specific conditions, there is potential for cyanides to interact with lactoferrin through primary amines (lysine) or histidine or thiol chemistry. However, this reaction is almost certainly unlikely to happen given the pH conditions required for lactoferrin production (pH <6.5). Cyanide interactions are favoured only under limited alkaline conditions (>pH 8). Importantly it must be noted that the pH is continuously monitored through in-line pH meters throughout the process, with a targeted pH range of pH 5.5-6.5 for the liquid lactoferrin streams. The incoming RO water used in processing also has in-line pH monitoring to ensure it meets the required pH levels, with general levels of pH 5.7 and a target of below pH 6.0. This is a critical aspect to ensure successful Lf production, and therefore importantly, the pH environment is highly unfavorable with respect to either potential cyanide release or interaction with Lf.

ix. The inquiry from FDA on this matter has caused Synlait to review all aspects associated with the chemistry logic associated with ensuring ferrocyanide absence in Lf. As a consequence, we are altering the Synlait Specification RMIN00049 with the statement “use of this product as a processing aid in the manufacture of ingredients that may be used in the finishing of infant formula requires the test for ferrocyanide to record absent in the ingredient product”.

x. Furthermore, Synlait will actively assess alternative salts which do not contain ferrocyanide, for use in the manufacture of lactoferrin.

f. Removal of potential fat and fat soluble contaminants:
    i. As outlined in the body of the GRAS submission and in Question 4 of this response, Synlait notes that the use of food-grade starting materials in compliance with U.S. regulations for contaminants will minimise the levels of any fat soluble contaminants in Synlait bLf. The raw milk used at Synlait is subject to frequent testing as part of a regular Contaminants Monitoring programme (NCCP) which is run and administered by the New Zealand Government Ministry for Primary Industries (MPI). This programme involves random sampling by government approved agents and testing for registered agricultural compounds and veterinary medicines; unregistered or prohibited agricultural compounds and veterinary medicines; radionuclides; contaminants including: organochlorines; organophosphates; dioxin and dioxin-like PCBs; mycotoxins; migration chemicals from food contact materials including packaging; maintenance compounds; and possible adulterants.

    The contaminants monitoring programme is conducted annually and Synlait has not been notified of any reported detections in its raw milk samples over the years. As such, there is no historical data indicating the presence of pesticides, PCB's and dioxin contaminants in the dairy material used in the manufacture of Synlait bLf. This gives us confidence that, levels of lipophilic contaminants in the major raw material are compliant with the relevant U.S. regulations for contaminants.

    The commencement of the Synlait bLf manufacturing process requires a separation of the fat bearing component of the raw milk in order to ensure that the processing equipment integrity can be maintained. As there is a physical removal of the bulk milk fat component of the raw milk and therefore the great majority of any fat soluble contaminants contained therein, it can be concluded that the level of such contaminants in Synlait bLf will be in compliance with the relevant U.S. regulations based on historical and ongoing raw milk testing programmes.

    It should be noted that Synlait has never been notified of any positive results as part of this mandatory annual testing programme. As such, in line with the comments to question 3, as the fat component of the milk is removed by centrifugal separation technologies to a level below 0.1% fat, there are only trace levels of fat and therefore fat soluble contaminants contained in the skim milk starting material, further reducing risks associated with persistent lipophilic contaminants in Synlait bLf.
    ii. As per the response in 4 (f) i above, Synlait has no historical data for dioxins/furans in its bLF to enable comparisons to be made with European manufacturers data or compare to the European Commission Regulation (EU) No. 1259/2011.

5. Bioactivity of bLf:
    a. Antibacterial properties of bLf. (Note: yet to be completed)

b. Iron homeostasis and bLf. (Note: yet to be completed)

6. Confidentiality of information submitted in GRN 000669:
   Synlait has carefully reconsidered the status of information originally submitted as "confidential" in support of GRN 000669 and advises that it has updated the status of all but the Part 7: Appendix 6 CV's of the GRAS Panel to **non-confidential**, in order to provide transparency and support for the evaluation of the Notice.

   a. The confidential and availability of information in Appendices of Part 7 has been amended. Updated title pages for each of the Appendices are provided with this response. Only the information in Appendix 6 relating to the GRAS Panel members remains designated as Confidential, it also contains Personal information.
      Synlait concurs with OFAS in that information indicated "not generally available" but not designated confidential can be posted on the website.
   b. Personal privacy information.
      The disclosure of personal privacy information has been acknowledged in Part 1 of the Notice (page 18) and an amended copy of this page is provided with this response.
      Synlait has identified personal privacy information relating to the CV's of the GRAS Panel in Part 7: Appendix 6. An updated title page for Appendix 6 is provided with this response.
   c. As noted above the confidential status of information in Part 7 has been reconsidered and amended. Updated title pages for each of the Appendices of Part 7 hare provided with this response.
   d. The reference to the personal communication (page 91) with Bright Dairy has been inserted as a reference in the Bibliography. An amended copy of page 91, and an updated Bibliography reflecting this change is provided with this response. In addition, the status of the letter from Bright Dairy has been amended to non-confidential (Part 7 Appendix 5 page A5:2).
   e. The GRAS panel were requested only to consider information contained in the Notice, and did not consider any non-public safety-related data in drawing their conclusion. As stated (page 16) the GRAS Panel concluded that on the basis of this Notice "other qualified and competent scientists reviewing the same publicly available toxicological and safety information would reach the same conclusion". Due to the nature of their expertise, it is likely that several of the panel members may have access to lactoferrin information related to research that is not currently publicly available, however if that was the case there was no indication of any safety-related issues or concerns raised during the discussions outside of the scope of the information that is included in the Notice and is generally available.
   f. Inconsistent information. We apologise for the inconsistencies noted and anticipate these have now been addressed.

Please note that we acknowledge responses to questions 5a and b remain pending. In order to provide substantiated answers to the two questions we have been accessing and accumulating the necessary literature over the prior 10 working days, with the answers not yet fully prepared. The response to question 5 will be provided by the opening of business on Monday the 28th of November.

Please do not hesitate to request further details or clarification. We appreciate the opportunity to respond to your questions and will welcome further dialogue as required

Yours sincerely

Lynley N Drummond
Director

Drummond Food Science Advisory Ltd
1137 Drain Road,
RD 2, Leeston 7682
New Zealand

PART 1 SIGNED STATEMENTS AND CERTIFICATION

1.1 INTRODUCTION

Pursuant to the criteria detailed in 21 CFR§170 Subpart E – Generally Recognized as Safe (GRAS) Notice [81 FR 55047 (August 17, 2016)], Synlait Milk Ltd. (Synlait) hereby notifies the Food and Drug Administration that the use of bovine milk-derived lactoferrin (bLf) in milk-based term infant (birth to 12 months) and toddler (13 to 36 months) formulas under the intended conditions of use is exempt from the requirement of premarket approval requirements of the Federal Food, Drug, and Cosmetic Act because Synlait has determined that such uses are Generally Recognized As Safe (GRAS) through scientific procedures in accordance with 21 CFR§107.30 (a) and (b).

Synlait Milk Ltd. (Synlait) is submitting this GRAS notice for use of its bovine milk lactoferrin (bLf) in non-exempt (defined in 21 CFR§107.3) milk-based term infant formula and toddler formula as described in this document. This Notice is based on scientific procedures as described in the following sections, under the conditions of the intended use of bLf in infant formula and toddler formulas.

A comprehensive search of the scientific literature for use, safety and toxicity information on bLf in infant formula, toddler formulas, and other foods was conducted through (November 2015 to July 2016) and made available to the GRAS Panel. The GRAS Panel, independently and critically, evaluated materials submitted by Synlait and other information deemed appropriate or necessary. Synlait accepts responsibility for the GRAS notice that has been made for bLf as described herein. Following an independent, critical evaluation, the GRAS Panel conferred and unanimously agreed to the conclusion described herein. Synlait is also of the opinion that other qualified and competent scientists, reviewing the same publicly available toxicological and safety information, would reach the same conclusion.

Synlait hereby certify, that to the best of our knowledge, this GRAS Notice is a complete, representative, and balanced submission that includes both unfavorable information, together with favorable information, known to Synlait and pertinent to the evaluation of the safety and GRAS status of bLf and it intended uses. Synlait is of the view that the notified substance, bLf, is not subject to the premarket approval requirements of the Federal

1.7 AVAILABILITY OF INFORMATION

The data and information that are the basis for Synlait's conclusion of the GRAS status of bLf under the intended conditions of use are available for the FDA's review, both during or after the evaluation of this Notice. Upon request, a complete copy of the data and information will be provided to the FDA either in an electronic format that is accessible for FDA evaluation, or on paper. Upon request, the data and information are available for the FDA to review and copy during customary business hours at either of the following addresses:

Lynley Drummond
Drummond Food Science Advisory Ltd,
1137 Drain Road, Killinchy,
RD 2, Leeston 7682 New Zealand
lynley_dfsa@me.com
Telephone: + 64 3 324 7284

Or,

Synlait Milk Ltd
1028 Heslerton Road,
RD 13,
Rakaia 7783
NEW ZEALAND
info@synlait.co.nz

Synlait acknowledges this Notice contains personal privacy information relating to individuals who have prepared and are responsible for this Notice, and that these individuals are aware of this disclosure and the implications under 21 CFR § 21.

Synlait has identified Confidential and not generally available and personal privacy information relating to members of the GRAS Panel that is presented in Part 7: Appendix 6 which it considers are exempt from disclosure under the Freedom of Information Act, 5 U.S.C. §552. Synlait has not identified any trade secrets included as a part of this Notice and authorizes for all information within this Notice to be provided to the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture, as required.

2.5 FINISHED PRODUCT SPECIFICATIONS

Specifications (Table 2-5), batch data for 5 batches manufactured between February 2015 and February 2016 (Table 2-7) and stability data (Table 2-10), are presented below for the Synlait manufactured bLf. To demonstrate conformance with the food-grade specifications, Synlait analyzed several batches of bLf. Analytical results from five lots (Table 2-7) suggest that Synlait's bLf is consistently manufactured to meet the standard specifications. The specification parameters comprise physical appearance, purity, total bLf levels, moisture, etc., as well as limits for potential chemical and microbiological impurities, and contaminants. A comparison of Synlait's bLf specifications to those of bLf that was the subject of GRAS notified substances reviewed by the FDA without any questions [including GRN 465 (Morinaga, 2014) and GRN 464 (Morinaga, 2014)] demonstrate that the bLf that is the subject of this GRAS Notice is substantially equivalent to the bLf that was the subject of those GRNs.

The presence of endotoxins (LPS) in commercial bLf has been identified as a potential inhibition factor for bioactivity (as discussed in 2.3). Synlait regularly monitors the endotoxin levels in the bLf finished product, and works towards continuous improvement in endotoxin levels (Table 2-9). Typical results for endotoxin levels are presented in Table 2-9 for batches manufactured between May 2014 and June 2015. Endotoxin measurement is completed by an independent test facility, Callaghan Innovation, a New Zealand Government Research Institute that includes accredited test analytical facilities (www.callaghaninnovation.govt.nz/). Endotoxin levels are measured using the FDA approved (www.fda.gov/ICECI/Inspections/InspectionGuides/InspectionTechnicalGuides/ucm072918.htm) *Limulus* Amebocyte Lysate (LAL) method (U.S. Pharmacopeial Convention, 2016). The average endotoxin level from Table 2-9, is 4.6 EU /mg BLf (average CV <5%). This average is halved to 2.3 EU/mg if the 2 results from the single batch of 1410001141 are omitted. Using the overall average value of 4.6 EU/mg, this equates to a potential contribution of endotoxin in infant formula of 4.6 EU per gram of infant formula powder. In an survey of 75 infant formula from 7 countries (31 formula brands), Townsend, Caubilla Barron, Loc-Carrillo, and Forsythe (2007) found the endotoxin levels in formula ranged from 40 to 5.5 x 10^4 EU per gram of formula powder using the LAL assay. The lower values of that range are consistent with the endotoxin levels in reconstituted infant formula (3.29 to 5.01 EU/mL) recorded by Lönnerdal et al. (2011). Ando et al. (2010) reported the endotoxin level of commercially available human lactoferrin as ranging between 15-26 EU/mg of protein.

Table 2-5. Manufacturing Specifications for Synlait Milk-derived Bovine Lactoferrin

Parameter	Specification	Method
Appearance	Pink to tan colored, free-flowing powder	Visual inspection
Foreign Matter	Absent / 25g	AS2300.4.5:1994
Sediment (/25 g)	A	ADMI Bull. 916 1990
pH (2% solution)	5.2 – 7.2	BS770:1986, ISO 7238 / IDF 104:2004, IDF 115A:1989, APHA (17th Edition) Ch. 15
Total Protein	≥95.0 %m/m	ISO 8968-1 / IDF 20-1:2001, AOAC 991.2
Lactoferrin (Purity)	≥95.0 % of protein	RP-HPLC with UV-Vis Detection at 220 nm (In House Method: TCH-05-0009)
Ash	≤1.3 %m/m	BS 1741:1988 (modified), BS 1743:1968 (modified)
Moisture	≤4.5 %m/m	IDF 26A: 1993
Iron Content	≤200 mg/kg	Acid Digest, ICP OES
Iron Saturation	≤20%	In house method (TCH-05-0011)
Heavy metals	<10 mg/kg	Acid Digest, ICP MS
Lead (Pb)	<0.15 mg/kg	Wet oxidation ICP MS
Cadmium (Cd)	<0.1 mg/kg	Wet oxidation ICP MS
Mercury (Hg)	<0.1 mg/kg	Wet oxidation ICP MS
Arsenic (As)	<0.02 mg/kg	Wet oxidation ICP MS (Detectable Limit)
Solubility		
Transmittance (2% solution, 600nm at 20°C)	80-100%transmittance Transparent (Visual assessment)	In house method (2% solution, 20°C) TCH-05-0010
Microbiological Tests		
Aerobic Plate Count	<1000cfu/g	ISO 4833
Coliforms	Not detected/g	ISO 11866-1/IDF 170-1

Table 2-5. Manufacturing Specifications for Synlait Milk-derived Bovine Lactoferrin

Parameter	Specification	Method
E. coli	Not detected/g	ISO 11866-1/IDF 170-1
Coagulase positive *Staphylococcus aureus*	Not detected/g	ISO 6888-3:2003
Yeasts and Molds	<10 cfu/g	ISO 6611/IDF 94:2004
Salmonella	Not detected /250g	ISO 6579
Enterobacteriaceae	Not detected/g	ISO 21528-1:2004
Chronobacter sakazakii	Not detected /300g	ISO/TS 22964 / IDF/RM 210:2006 (see Appendix 3, pg. A3: 20)
Aluminum	<4.8 mg/kg	Wet oxidation ICP-MS
Nitrates	≤50 mg/kg	NZJDST 15, 83-90, 1980, ISO 14673-2, IDF 189-2, AOAC 968.07 (mod)
Nitrites	≤2 mg/kg	NZJDST 15, 83-90, 1980, ISO 14673-2, IDF 189-2, AOAC 968.07 (modified)
Melamine	<0.1 mg/kg	LC-MS/MS (Detectable limit)
Aflatoxin M1	<0.5 µg/kg	AOAC 971.22 (1998) (modified)

Abbreviations:

AOAC Association of Official Analytical Chemists
APHA American Public Health Association
BS British Standards
ICP MS Inductively Coupled Plasma Mass Spectrometry
ICP OES Inductively Coupled optical Emission Spectrometry
HPLC High Performance
Liquid Chromatography
IDF International Dairy Federation
ISO International Organization for Standardization
TCH Technical Manual

Table 2-7. Batch Data of Synlait Milk-derived Bovine Lactoferrin

Specification Parameter	**Limit**	**Batch Nos**				
		LFN1510001209	LFN1510001130	LFN1510000679	LFN1510000948	LFN1610000308
Appearance	Pink to tan, free-flowing	Typical	Typical	Typical	Typical	Typical
Foreign Matter (in 25g)	Absent /	Absent	Absent	Absent	Absent	Absent
Sediment (/25 g)	A	A	A	A	A	A
pH (2% solution)	5.2 – 7.2	6.10	5.80	5.90	5.92	5.79
Total Protein (%m/m)*	≥95.0	97.1	96.9	96.6	97.0	96.9
Lactoferrin (% protein)	≥95.0	95.3	97.4	96.8	96.5	96.3
Ash (%m/m)	≤1.3	<0.1	0.2	0.2	0.1	0.4
Moisture (%m/m)	≤4.5	3.6	3.5	4.2	4.1	4.1
Iron Content (mg/kg)	≤200	110	110	110	110	110
Iron Saturation (%)	≤20	11.0	11.0	11.0	11.0	11.0
Minerals						
Sodium (mg/100g)		63	64	84	51	30
Potassium (mg/100g)		<0.91	<0.91	<0.91	<0.91	<0.91
Magnesium (mg/100g)		<0.84	<0.14	<0.14	<0.14	<0.14
Phosphorus (mg/100g)		2.6	2.5	4.5	2.7	0.84
Calcium (mg/100g)		1.2	0.75	1.7	1.5	2.8
Chloride (%m/m)		0.845	0.838	0.824	0.788	1.0
Copper (µg/100g)		<11	22	20	<11	14
Zinc (mg/100g)		0.42	0.39	0.72	0.53	0.57
Manganese (µg/100g)		<0.14	<7	8.1	<7	<7

Table 2-7. Batch Data of Synlait Milk-derived Bovine Lactoferrin

Specification Parameter	**Limit**	**Batch Nos**				
		LFN1510001209	LFN1510001130	LFN1510000679	LFN1510000948	LFN1610000308
Heavy metals						
Lead (Pb) (mg/kg)	<0.02	<0.01	<0.01	<0.01	<0.01	<0.01
Cadmium (Cd) (mg/kg)	<0.1	<0.002		<0.002	<0.002	<0.002
Mercury (Hg) (mg/kg)	<0.1	<0.01	<0.01	<0.01	<0.01	<0.01
Arsenic (As) (mg/kg)	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02
Aluminium (mg/kg)	<1	<1	<1	<1	<1	<1
Solubility (2% solution, 600 nm at 20°C)	Transparent	Transparent	Transparent	Transparent	Transparent	Transparent
% Transmittance (2% solution, 600 nm at 20° C)	80-100	96.0	95.8	94.7	97.9	95.2
Microbiological Tests						
Aerobic Plate Count (cfu/g)	<1000	<10	<10	<10	<10	<10
Coliforms (in 1g)	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
E. coli	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
Coagulase positive *Staphylococcus aureus* (in 1g)	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
Yeasts and Molds (cfu/g)	<10	<1	<1	<10	<10	<10
Salmonella (in 250 g)	Absent	Absent	Absent	Absent	Absent	Absent
Chronobacter sakazakii (in 300g)	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
Aflatoxin M1	<0.5	<0.025	<0.025	<0.025	<0.025	<0.025

*%m/m = % mass/mass

and bLf groups compared to the control formula group. The results of this trial show that bLf supplemented formula supports the growth and development of infants.

In a recently completed clinical trial (NCT02239588) evaluating the effects of an infant formula (0-6 months) manufactured by Synlait Milk Ltd., containing bLf at 60 mg/100g, normal growth and development was observed and the formula was well tolerated (Bright Dairy Ltd., 2016) (Appendix 5, pg. A5: 2). Quantitative details of the growth and tolerability studies are not available at this time. Published aspects of the study, involving exclusive consumption of the formula, showed beneficial effects on the infants' fecal microbial profile, and the concentrations of fecal short chain fatty acids (Liu et al., 2016). At the time of the study, Synlait did not manufacture the bLf used to make the commercial formula. However, a comparison of the specifications of the bLf used in the formula with the specifications of Synlait's bLf indicate that they are essentially equivalent. Since 2014, the commercial formula has contained bLf manufactured by Synlait. The formula has been sold and consumed in China without any reported adverse effects attributable to the bLf.

In a large multi-center, double blind, parallel-designed, gender-stratified prospective study (Johnston et al., 2015) 480 infants were randomized to receive a commercial cow's milk-based formula (control, n=155) or one of 2 test formulas with bLf at 0.6 g/L (LF0.6, n=165) or bLf at 1.0 g/L (LF1.0, n=116). The concentrations of bLf in the test formulas are within the range of lactoferrin concentration in human milk. The test formula also contained a proprietary prebiotic mix of polydextrose and galactooligosaccharides, and adjusted arachidonic acid levels. The primary outcome for the study was growth rate from 14 to 120 days of age, with growth monitored over the duration of the study through to 1 year. No statistically significant differences were observed for growth rate from day 40-120. With the exception of one non-clinically significant difference in head circumference observed in females between the LF1.0 and control group (day 14-60), no other significant differences were observed for mean achieved weight, length or head circumference at any point up to day 365. Mean achieved weight for males and female were within the 25^{th} and 75^{th} percentiles of the WHO weight-for-age growth charts from days 14-365. Acceptance and tolerance of test formulas was good, with no significant differences detected in fussiness, gassiness, or mean stool frequency at all time points. This study provides support for the safety, tolerance and associated normal growth of healthy term infants consuming formula containing bLf at levels of up to 1.0 g/L.

King et al. (2007) examined the impact of long-term feeding of a bLf supplemented infant formula on growth, hematologic and immune parameters and the impact on childhood illnesses in term or near term healthy infant. Infants, who were strictly bottle-fed, and were enrolled between 0 and 4 weeks of age, were randomized to receive either control formula (Similac with

7.2 REFERENCES

All references are generally available

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PART 7:
APPENDIX 1: Raw Material And Packaging Specifications

The data and information presented within Appendix 1 is **generally available**.

Document Information

Product Name	:	Lactoferrin Powder		
Prepared by	:	Arnab Sarkar	Status :	Approved
Supersedes	:	NA		

Product Identification

This product can be identified in various systems as the following:

System Name	System ID	Coding
Synlait ERP	M3	LFN05105

Product Attributes

Description	:	95% Protein, pasteurised, spray dried lactoferrin, pink to tan, free flowing powder.
Product descriptor	:	Lactoferrin (38)
Allergen(s)	:	Dairy Product
Traceability	:	Production lot record
Ingredients	:	Lactoferrin

General Composition

Parameter	Unit	Typical	Min	Max	Test Method
Protein as is	%m/m		95		ISO 8968-1 / IDF 20-1:2001, AOAC 991.20
Lactoferrin	% Protein		95		HPLC method (In House Method: TCH-05-0009)
Ash	%m/m			1.3	BS 1741:1988 (modified), BS 1743:1968 (modified)
Moisture	%m/m			4.5	IDF 26A: 1993
Iron	mg/kg			200	Acid Digest, ICP OES
Iron Saturation	%			20	In house method (TCH-05-0011)

Physical and Chemical Attributes

Parameter	Unit	Typical	Min	Max	Test Method
Sediment	/25g	A	A	A	ADMI Bull. 916 1990
Foreign matter	/25g	Absent		Absent	AS 2300.4.5:1994
pH		6.0	5.2	7.2	BS770:1986, ISO 7238 / IDF 104:2004, IDF 115A:1989, APHA (17th Edition) Ch 15
Solubility		Transparent			In house method (2% solution, 20°C) TCH-05-0010

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RD13, Rakaia 7783
New Zealand
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Sensory Attributes

Parameter	Description	Test method
Appearance	pink to tan, free flowing powder	Visual Observation

Microbiological Standards

Parameter	Unit	Max.	Test method
Aerobic Plate Count	cfu/g	1000	ISO 4833:2003
E.coli	/g	Not detected	ISO 11866 – 1:2005 (E)/IDF 170-1 :2005 (E) (mod)
Yeast and moulds	cfu/g	10	ISO 6611/IDF 94:2004
Salmonella	/250g	Not detected	ISO 6579:2002 (E)
Coagulase Positive Staphylococcus	/g	Not detected	ISO 6888-3:2003
Coliform	/g	Not detected	ISO 4832:2006
E.sakazaki	/300g	Not detected	ISO/TS 22964 / IDF/RM 210:2006
Enterobacteriaceae	/g	Not detected	ISO 21528-1:2004

Contaminants and Residues

Parameter	Unit	Limit	Test method
Nitrates	mg/kg	≤50	NZJDST 15, 83-90, 1980, ISO 14673-2, IDF 189-2, AOAC 968.07 (mod)
Nitrites	mg/kg	≤2	NZJDST 15, 83-90, 1980, ISO 14673-2, IDF 189-2, AOAC 968.07 (mod)
Heavy Metals	mg/kg	<10	Acid Digest ICPMS
Melamine [1]	ppm	<0.1	LC-MS/MS **(Detectable limit)**
Arsenic [1]	mg/kg	<0.02	Wet oxidation ICP MS **(Detectable Limit)**
Aluminium	mg/kg	<4.8	Wet oxidation ICP-MS
Cadmium	mg/kg	<0.1	Wet oxidation ICP-MS
Mercury	mg/kg	<0.1	Acid Digest ICPMS
Lead	mg/kg	<0.15	Wet oxidation ICP MS
Aflatoxin M1	µg/kg	<0.5	G Barbieri et al, J Food Sci, 59 (1994) p1313-

[1] to be reported as "Not Detected" on the COA

Product Statements

This product complies with the following requirements:

General spec	Spec descriptions
	HALAL
	GMO-free

This product is manufactured and packed according to Synlait RMP requirements

Synlait Milk Ltd
1028 Heslerton Road
RD13, Rakaia 7783
New Zealand
P +64 3 373 3000
www.synlait.com

Packaging

Packaging materials	Descriptions
Foil bag	5 kg – Laminated foil quad pouch (polyester 12 µm/foil 7 µm/PE 130 µm)
Carton	2 x 5 kg bags – RSC STC 510*380*160
Pallet detail	30 carton per pallet

Labelling Information

Each bag is pre-printed with	Synlait ™ Spray Dried Lactoferrin Net weight 5 kg Product of New Zealand Registration Number – 540 Address details Storage details Pasteurised product Fit for human consumption
Each bag is labelled with	Production date and best before date Bag Number Lot number
Each Carton is pre-printed with	Synlait ™ Spray Dried Lactoferrin Net weight 10 kg Product of New Zealand Registration Number – 540 Address details
Each Carton is labelled with	Store cool, dry, ventilated Production date Lot number Carton Number Units per Carton: 2 bags

Storage

Shelf life	:	36 months
Storage instructions	:	Temperature < 25 °C Relative humidity <65% Store in cool, dry, and well ventilated place Stored off the floor and away from walls once opened use within 1 month

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Revision History

Version	Nature of Change	Initiated by	Approved by	Date dd-mm-yyyy
1	New spec.	Arnab S.	Tom A.	04-03-2014

Synlait Milk Ltd
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FDA COMPLIANCE

All FSI polypropylene filtration media product lines are manufactured using FDA compliant materials under the Federal Food, Drug, and Cosmetic Act under regulations:

21 C.F.R. 177.1520 (c) 1.1
21 C.F.R. 177.2800
21 C.F.R. 178.3400

Provided that the end user is complying with FDA's good manufacturing practices under Title 21 C.F.R. 174.5.

Quality Assurance Manager

5/30/13
date

KOCH MEMBRANE SYSTEMS

KMS HFK™-131 FOOD & DAIRY UF ELEMENTS

Ultrafiltration 4", 6" and 8" Spiral Element Series

PRODUCT DESCRIPTION

Membrane Chemistry:	Proprietary semi-permeable polyethersulfone (PES)
Membrane Type:	HFK™-131 with observed separation range of 10,000 Daltons
Construction:	Sanitary spiral wound element with net outer wrap
Regulatory Status:	Conform to USDA 3-A standards and FDA regulations (CFR Title 21)
Options:	Diameter: 3.8", 4.3", 6.3", 6.4", 8.0", or 8.3"
	Length: 33", 35.5", or 38"
	Feed Spacer: N (31 mil), V (46 mil), H (62 mil), or F (80 mil), D (100 mil)
	Outer wrap: Controlled (e.g. NYV) or trimmable (e.g. NYT)

SPECIFICATIONS

Model	Active Membrane Area									
	NYV/T Spacer (31 mil)		VYV/T Spacer (46 mil)		HYV/T Spacer (62 mil)		FYV/T Spacer (80 mil)		DYV/T Spacer (100 mil)	
	ft^2	(m^2)	ft^2	(m^2)	ft^2	(m^2)	ft^2	(m^2)	ft^2	(m^2)
3838 HFK-131	72	(6.7)	58	(5.4)	45	(4.2)	-	-	-	-
4333 HFK-131	93	(8.6)	73	(6.8)	55	(5.1)	44	(4.1)	-	-
4336 HFK-131	95	(8.8)	79	(7.3)	59	(5.5)	-	-	-	-
4338 HFK-131	102	(9.5)	81	(7.5)	-	-	-	-	-	-
6338 HFK-131	228	(21.2)	180	(16.7)	142	(13.2)	119	(11.1)	102	(9.5)
6438 HFK-131	228	(21.2)	180	(16.7)	142	(13.2)	119	(11.1)	-	-
8038 HFK-131	358	(33.2)	276	(25.6)	215	(20.0)	-	-	-	-
8338 HFK-131	-	-	308	(28.6)	241	(22.4)	194	(18.0)	-	-

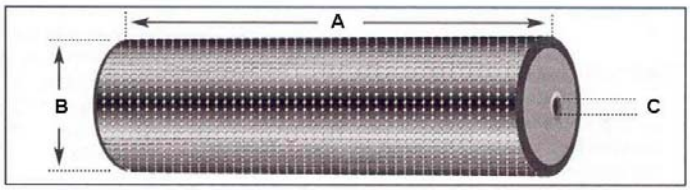
Not all combinations are available.
6438 elements are only available in controlled configuration. 6338 elements are only available in trimmable configuration.

OPERATING AND DESIGN INFORMATION*

Typical Operating Pressure:	30 - 120 psi (2.1 - 8.3 bar)
Maximum Operating Pressure:	140 psi (9.7 bar)
Operating Temperature Range:	41 - 131°F (5 - 55°C)
Cleaning Temperature Range:	105 - 122°F (40 - 50°C)
Allowable pH - Continuous Operation:	2.0 - 10.0
Allowable pH - Clean-In-Place (CIP):	1.8 - 11.0
Design Pressure Drop Per Element:	N spacer: 12-15 psi (0.8-1.0 bar)
	V spacer: 15-20 psi (1.0-1.4 bar)
	H or F spacer: 15-25 psi (1.0-1.7 bar)
Design Pressure Drop Per Vessel (3 in series):	N spacer: 36-45 psi (2.5-3.1 bar)
	V spacer: 45-60 psi (3.1-4.1 bar)
	H or F spacer: 45-75 psi (3.1-5.2 bar)
Design Pressure Drop Per Vessel (4 in series):	N spacer: 48-60 psi (3.3-4.1 bar)
	V spacer: 60-68 psi (4.1-4.7 bar)

* Consult KMS Process Technology Group for specific applications.

NOMINAL DIMENSIONS



Model	A inches (mm)	B inches (mm)	C inches (mm)
3838 HFK-131	38.0 (965)	3.8 (96)	0.831 (21.1)
4333 HFK-131	33.0 (838)	4.3 (109)	0.831 (21.1)
4336 HFK-131	35.5 (902)	4.3 (109)	0.831 (21.1)
4338 HFK-131	38.0 (965)	4.3 (109)	0.831 (21.1)
6338 HFK-131	38.0 (965)	6.3 (160)	1.138 (28.9)
6438 HFK-131	38.0 (965)	6.4 (162)	1.138 (28.9)
8038 HFK-131	38.0 (965)	7.9 (201)	1.138 (28.9)
8338 HFK-131	38.0 (965)	8.3 (211)	1.138 (28.9)

Note: Not all combinations are available.

Membrane Characteristics:

- The membrane used in these modules consists of a semipermeable polyethersulfone (PES) layer on a polyester backing material.
- Pure water flux of these PES HFK-131 membranes is 1.0-2.2 gfd/psi (24-53 l/m²/h/bar) at 77°F (25°C).
-

Operating Limits:

- **Operating Pressure:** Maximum operating pressure is 140 psi (9.7 bar).
- **Permeate Pressure:** Permeate pressure should not exceed baseline (concentrate) pressure at any time (including on-line, off-line and during transition). Reverse pressure will damage the membrane.
- **Differential Pressure:** The maximum differential pressures per element are listed on the front of this document, including design values for multi-element housings.
- **Temperature:** Maximum operating temperature is 131°F (55°C). Maximum cleaning temperature is 122°F (50°C).
- **pH:** Allowable range for continuous operation is 2.0 to 10.0. Allowable pH range for cleaning is 1.8 to 11.0.

Water Quality for Cleaning & Diafiltration:

- **Turbidity and SDI:** Maximum feed turbidity is 1 NTU. Maximum feed SDI is 5.0 (15-minute test).
- **Guidelines:** Please refer to the KMS "Water Quality Guidelines for CIP and Diafiltration" for more detailed information.

Chlorine and Chemical Exposure:

- Adherence to cleaning and sanitizing procedures including chemical concentrations, pH, temperature, and exposure time is necessary to achieve maximum useful element life. Accurate records should be maintained.
- KMS standard cleaning procedures for dairy applications should be followed. Recommended chlorine exposure time at the defined conditions is 30 minutes per day.
- Residual chlorine concentration during cleaning cycle (CIP) should be 150 ppm @ pH 10.5 or higher. Chlorine concentration should never exceed 200 ppm.
- Chlorine should only be added to the cleaning solution after the pH has been adjusted to 10.5 or higher.
- Iron or other catalyzing metals in the presence of free chlorine or hydrogen peroxide will accelerate membrane degradation.
- Sanitizing should be done only after a complete cleaning cycle and with water of acceptable quality. Refer to cleaning instructions and feedwater quality technical bulletins.

Cationic Polymers and Surfactants:

HFK-131 membranes may be irreversibly fouled if exposed to cationic (positively charged) polymers or surfactants. Exposure to these chemicals during operation or cleaning is not recommended and will void the warranty.

Lubricants:

For element installation, use only water or glycerin to lubricate seals. The use of petroleum or vegetable-based oils or solvents may damage the element and will void the warranty.

Supplemental Technical Bulletins:

- UF Element Cleaning Procedures
- Water Quality Guidelines for CIP and Diafiltration

Service and Ongoing Technical Support:

KMS has an experienced staff available to assist end-users and OEM's for optimization of existing systems and development of new applications. KMS also offers a complete line of KOCHKLEEN® membrane pretreatment, cleaning, and maintenance chemicals.

KMS Capability

KMS is the leader in crossflow membrane technology, manufacturing reverse osmosis, nanofiltration, microfiltration, and ultrafiltration membranes and membrane systems. The industries we serve include food, dairy and beverage, semiconductors, automotive, water and wastewater, chemical and general manufacturing. KMS adds value by providing top quality membrane products and by sharing our experience in the design and supply of thousands of crossflow membrane systems worldwide.

Koch Membrane Systems, Inc., www.kochmembrane.com
Corporate Headquarters: 850 Main Street, Wilmington, Massachusetts 01887-3388, USA, Tel. Toll Free: 1-888-677-5624, Telephone: 1-978-694-7000, Fax: 1-978-657-5208
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• Melbourne, Australia • Singapore • Sao Paulo, Brazil • Manama, Kingdom of Bahrain

Document Information

Material Name	:	Cheese Salt
Prepared by	:	Jo Steven
Supersedes	:	V3

Status :

Draft	Approved
	X

Material Identification

This product can be identified in various systems as the following:

System Name	Item name (as per M3)	Coding
Synlait ERP	Cheese Salt	RMIN00049
Dominion Salt	-	PDV Cheese Grade Salt

Material Attributes

Description	:	Pure dried vacuum (PDV) salt, with anticaking agent sodium ferrocyanide (E535). **Note: Anticaking agent not allowed for use for infant products**
Alternative name	:	Sodium Chloride, NaCl
Supplier	:	Dominion Salt, New Zealand; Production Site: Lake Grassmere (LG), or Mt Maunganui (MM)
Allergen(s)	:	None
Contains Dairy Material	:	No
Traceability	:	Production Batch
Grade	:	Food Grade
Ingredients	:	Salt, Sodium Ferrocyanide (E535)

Documentation Requirements

This product needs to comply with following requirements:

Documents Required	Frequency
Certificate of Analysis (CoA)	Every shipment
HALAL	On request
KOSHER	On request
GMO-free certificate/ declaration	On request
MSDS	On request
Allergen documentation	On request
Dairy material declaration as required (SOR / FIC & accompanying Health Cert.) Must contain the following attestations: Were derived only from animals and processed in countries which are recognised by the OIE World Organisation for Animal Health as free of foot and mouth disease, with or without vaccination; Were derived only from animals which meet OIE requirements for lumpy skin disease, sheep pox and goat pox freedom; The country of origin has controls in place to ensure that only healthy animals are used for milk production	N/A
Other technical documents	On request
Packing list	Every shipment

This product needs to be manufactured and packed according to HACCP regulations

General Composition

Parameter	Unit	Typical	Min	Max	Required on CoA	Comment	Testing plan (Synlait)*
Sodium Chloride	% DM		99.6		On Request	Monthly Monitoring	High + SL
Moisture	%			0.2	Yes	-	Low
Sodium Ferrocyanide	ppm			15	Yes	May be reported on CoA as Anticaking Agent $[Fe(CN)_6]^{4-}$	Low
Matter insoluble in water	ppm			300	On Request	-	Low

Physical and Chemical Attributes

Parameter	Unit	Typical	Min	Max	Required on CoA	Comment	Testing plan (Synlait)*
Scorched Particles (Black specks)	Disc/50g			A	Yes	ADMI Method. May be reported on CoA as visual foreign matter	Low
Other Foreign Matter	/50g		Absent		Yes	May be reported on CoA as unacceptable foreign matter absent	Low
Particle size passing 212µm	%			2	Yes	-	N/A
Particle size passing 850µm	%		100		Yes	-	N/A

Sensory Attributes

Parameter	Description	Required on CoA	Testing plan (Synlait)*
Appearance	White, relatively coarse uniformly sized crystals. No caking that does not break up under moderate pressure.	On Request	High (Internal Evaluation) + SL
Odour	Odourless - no foreign or off-odours	On Request	High (Internal Evaluation) + SL

Contaminants and Residues

Parameter	Unit	Limit (Max)	Required on CoA	Comment	Testing plan (Synlait)*
Cadmium (Cd)	mg/kg	0.2	Yes	Yearly Monitoring	Low
Arsenic (As)	mg/kg	0.5	Yes	Yearly Monitoring	Low
Copper (Cu)	mg/kg	2	On Request	Monthly Monitoring	N/A
Iron (Fe)	mg/kg	10	On Request	Monthly Monitoring	N/A
Lead (Pb)	mg/kg	1	Yes	Yearly Monitoring	Low
Mercury (Hg)	mg/kg	0.05	Yes	Yearly Monitoring	Low
Alkalinity (as Na_2CO_3)	mg/kg	300	On Request	Monthly Monitoring	N/A

*Test plan for Synlait RM test procedure: high = test every time; low = reduced test can be used when applicable; N/A: not tested (e.g. due to test method capability); +SL= tested when shelf-life extension is required.

Packaging

Pack Size	Descriptions
25 kg	Plastic (Polyethylene) Bag. Packaging must be suitable for food contact.

Labelling Information

This information is required on the label in accordance with the Australia New Zealand Food Standards Code:

- Product name
- Manufacturer's name and address
- Ingredient list (if applicable) – on the label or in accompanying documentation
- Date of manufacture
- Expiry or Best Before Date
- Weight or quantity
- Lot/batch number

Storage Requirements

Shelf life - unopened	:	60 months (5 years) from date of manufacture
Storage instructions	:	Store in dry, cool conditions, away from direct sunlight in original sealed packaging.
Shelf-life - opened	:	Shelf life = first opening date + 6 months OR original manufacturer shelf life, whichever is shortest. Must be stored in well-sealed foil pouch at recommended temperatures. Pre-weighed: max. 14 days when stored protected from light (in black plastic bag or similar) at recommended temperature.

Logistic Requirements

Method of shipping(s)	:	Road / Sea freight
Estimated lead time	:	2 - 4 weeks
Shipping requirement(s)	:	CoA and packing slip to accompany goods

Revision History

Version	Nature of Change	Initiated by	Approved by	Date dd-mm-yyyy
1	New Specification	KW	IH	07/09/12
2	Amend contaminant levels in accordance to GB update and customer requirement	KW	IH	08/02/13
3	Add new supplier. Ensure has both FCC and GB requirements	KW	TJ	17/04//15
4	Update information into new template and update suppliers. Add foreign matter requirements. Align units with current CoA	JS	TJ	23/11/15

PRODUCT SPECIFICATION

(Appendix 2 of the NZDI Salt Specification)

PURE DRIED VACUUM SALT (PDV)

Head Office & N.I. Refinery

89 Totara Street, Mount Maunganui, New Zealand
PO Box 4249, Mount Maunganui South
Phone: 64 7 5756193 Fax: 64 7 575 3017
Email: sales@domsalt.co.nz
Website: www.domsalt.co.nz

Lake Grassmere & S.I. Refinery

Kaparu Road, Marlborough, New Zealand
PO Box 81, Seddon
Phone: 64 3 575 7021 Fax: 64 3 575 7002
Email: sales@domsalt.co.nz
Website: www.domsalt.co.nz

CHEESE SALT			
COMPONENTS	**NZ Dairy Salt Specification**	**TYPICAL**	**DSL Test Method** *(Reference Method)*
Sodium Chloride as NaCl - Minimum moisture free	Min 99.6 %	>99.8%	Calculated by difference
Moisture Content	Max 0.2%	0.02%	DSL Pt. 12 *(BS 7319:Part 2:1990)*
Matter Insoluble in water	Max 300 mg/kg	<10 mg/kg	DSL Pt. 11 *(BS 7319:Part 3:1990)*
Foreign matter[1]	ADMI - A	A	DSL Pt. 8 *(In-house)*
Sulphate as Na_2SO_4	Max 3000 mg/kg	<1500 mg/kg	DSL Pt. 14 *(BS 7319:Part 4:1990)*
Calcium as Ca	Max 100 mg/kg	<20 mg/kg	DSL Pt. 5 *(BS 7319:Part 5:1990)*
Magnesium as Mg	Max 100 mg/kg	<15 mg/kg	" "
Cadmium as Cd	Max 0.2 mg/kg	<0.01 mg/kg	DSL Pt. 4 *(BS 7319:Part 6:1990)*
Arsenic as As	Max 0.5 mg/kg	<0.01 mg/kg	DSL Pt. 2 *(BS 4404:1968)*
Copper as Cu	Max 2 mg/kg	<0.1 mg/kg	DSL Pt. 4 *(BS 7319:Part 7:1990)*
Lead as Pb	Max 1 mg/kg	<0.1 mg/kg	DSL Pt. 4 *(BS 7319:Part 8:1990)*
Mercury [2] as Hg	Max 0.05 mg/kg	<0.01 mg/kg	ICP *(BS 7319:Part 9:1990)*
Alkalinity as Na_2CO_3	Max 300 mg/kg	<100 mg/kg	DSL Pt. 1 *(BS 7319:Part 10:1990)*
Iron as Fe	Max 10 mg/kg	<1.0 mg/kg	DSL Pt. 4 *(BS 7319:Part 11:1990)*
Food Additives [3]:			
Additive 535 as $[Fe(CN)_6]^{4-}$	Max 15 mg/kg	4-6 mg/kg	DSL Pt. 9 *(BS 7319:Part 12:1990)*

Notes: < Less than > Greater than ppm = mg/kg = (**%** x 10,000)

1. "Foreign matter" is not defined in the FSANZ Code Volume 2, therefore reference "7CFR 2858.267 Scorched Particle Standards for Dry Milks" has been adopted to quantify the level of sediment. A photocopy of this reference is available on request to the Works Chemist.
2. Test performed on incoming bulk salt shipment before refining.
3. As specified in FSANZ Food Standards Code Volume 2, Part 1.3 schedule 1. (Available at website: www.foodstandards.govt.nz)

GRADE DESCRIPTION:

High purity certified vacuum salt especially prepared to be of relatively coarse crystals with a narrow grain size range. Strictly prepared in batch lots to optimise grain size uniformity. Suitable for salting in some mechanical cheese manufacturing plants using accurate pneumatic salt conveying equipment, which are sensitive to a wide or variable range of grain sizes.

Country of origin: Product of New Zealand

NUTRITIONAL INFORMATION

Component	Per 100g
Saturated Fat	Nil g
Mono Unsaturated Fat	Nil g
Poly Unsaturated Fat	Nil g
Trans Fatty Acids	Nil g
	Typically
Sodium	39.1g min
Chloride	60.5g min
Calcium	<0.4 - 4 mg
Potassium	2-4 mg
Iron	<1 mg
Cholesterol	Nil mg
Dietary Fibre – soluble	Nil mg
Dietary Fibre - Insoluble	Nil mg

GRAIN SIZE: 100% passing 850 microns
0 - 2% passing 212 microns

BULK DENSITY: Nominally: loose 1.25g/ml, compacted 1.43g/ml

COMPLIANCE:

- ***Certified to NZDI Salt Specification***
- Complies with BS998:1990 Vacuum Salt for Food Use
- Complies with FSANZ Food Standards Code Volume 2 Standard 2.10.2/Clause 2
- NOT a genetically modified food as defined under 1.5.2 of the FSANZ Standards Code Volume 2
- *Is Free from known Allergens*
- *Halal Certified*
- *Kosher Certified*
- *Dominion Salt is ISO 9001 certified*

PACK:

Bulk Bag Woven Polypropylene with Polyethylene liner (Weight by arrangement)
Bulk Bag Woven Polypropylene with Polyethylene barrier layer laminated to inside face of woven material.
25kg Polyethylene Bag (no outer)
Packaging material complies with US FDA regulations Title 21, parts 170-199
Print colour: Bulk Bag - Blue 072
25kg Bag - Spot Orange 021

Pallets:

Small packs: Standard pallet configuration is 48 x 25 kg bags (1.2 tonnes per pallet) The salt is stretch wrapped and capped on pallets with a pallet sheet between the pallet and the salt
Bulk Bags: Standard configuration is one bulk bag per pallet

Issue Date: 20.08.09
Issue No: 13

Raw Material Specification Synlait Skim Milk

	Month	Limits	September	March	June	September	March	June	Dec	Sept	Dec	Mar
	Year		2012	2013	2013	2013	2014	2014	2014	2015	2015	2016
Moisture	% m/m		90.69	90.34	90.98	90.67	90.02	90.84	90.58	90.82	90.53	90.63
Fat	% m/m	<0.15	<0.1	0.111	0.086	0.07	0.09	0.07	0.06	0.07	0.09	0.1
Protein	% m/m	>3.5	3.64	4.11	3.6	3.62	4.25	3.78	3.82	3.7	3.81	3.91
Lactose/carbo	% m/m		4.89	4.649	4.584	4.85	4.85	4.53	4.76	4.61	4.77	4.6
Ash	% m/m	<1.0	0.78	0.79	0.75	0.79	0.79	0.78	0.78	0.8	0.8	0.76
Total Solids (TS)	% m/m		9.31	9.66	9.02	9.33	9.98	9.16	9.42	9.18	9.47	9.37
MICRONUTRIENT												
Calcium	mg/100g	>100	130	140	130	140	140	130	140	120	130	130
Chloride	mg/100g	<200	96	102	106	90	100	107	95	89	94	102
Copper	ppm											<0.028
Copper	µg/100mL		7.8	5	7.5	4.1	3.2					
Iron	ppm		<0.025	0.027	<0.025	<0.025	0.023					<0.25
Iodine	ug/100g		7.5	4.7	15	5.2	4.8	10.0	6.2	0.09 mg/kg	3.5	3.6
Potassium	mg/100g		160	150	160	160	150	150	170	150	160	150
Manganese	mg/100g		<1.8	3.1	2.5	<1.75	3.3					<1.8 ug/100g
Magnesium	mg/100g		10	13	11	11	13	12	12	10	11	12
Sodium	mg/100g	<100	34	37	38	31	36	38	34	30	31	36
Phosphorus	mg/100g	<200	110	110	99	110	100	100	110	100	100	98
Selenium	mg/100g			1.5			1.5					1.3 ug/100g
Zinc	mg/100g		0.45	0.47	0.43	0.41	0.44	0.44	0.45	0.41	0.41	0.39
Vit B1 (Thiamine)	µg/100mL		<15.7	42.49	25.18	19.67	28.40	22.82	34.00	27.30	21.00	24.00
Vit B2 (Riboflavin)	µg/100mL		227	226	201	224	255	221	227	227	215	265
Vit B3 (Niacin)	µg/100mL			<150								
Vit B5 (Pantothenic Acid)	µg/100mL		351	200	400	500	400	500	500		0.42 mg/100g	226
Vit B6 HCl	µg/100mL		29	33	33	28	32.0	30.5	39.0	29	35	32
Vit B12	µg/100mL		0.42	0.578	<0.2	0.51	0.529	0.656	0.537	0.5	0.587	0.558
Vit C	mg/100mL		<1	<1	<1	<1						
Biotin	µg/100mL		<8	<8		<8						
Total L-Carnitine	mg/100g		2.34	1.84	1.5	1.7	2.4	2.7	1.9	2.6	1.5	2.5
Choline	mg/100mL		10	13	11	11	5.7	15.0	11	9	10	9.25
Folic acid	µg/100mL			<8	<8							
Inositol	mg/100g		4.8	4.5	4.2	4.3	4.9	5.6	5	5.4	6.5	6.15
CONTAMINANT												
Total Heavy Metals	mg/kg	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
Nitrate	mg/L	<1	0.1	<1	<1	<0.2	0.4	0.4	<0.2	<0.2	<0.2	<1
Nitrite	mg/L	<1	0.01	0.1	0.08	0.09	0.05	0.05	0.04	0.03	0.05	<0.03
Inhibitory substances	IU/mL	<0.0025	<0.0025	<0.0025	<0.0025	<0.0025	<0.0025	<0.0025		<0.0025		

Table 1 – Processing Aid Comparison Morinaga vs Synlait Bovine Lactoferrin

Table 2. Processing Aids and Chemicals Used in the Production of Cow's Milk-Derived Lactoferrin (cMDLf) - Page #10 (27 of 217) from GRAS 465.pdf			**Synlait Milk Ltd Spray Dried Bovine Lactoferrin**	
Processing Aid or Chemical	**Manufacturer**		**Processing Aid or Chemical**	**Manufacturer**
	At Milei for cMDLf-1, cMDLf-2	**At Riedlingen for cMDLf-2**		
Demineralized water	Milei	Riedlingen plant	Demineralized water	In-house RO water
Sodium chloride (NaCl)	Herkommer & Bangerte	Herkommer & Bangerte	Sodium chloride (NaCl)	Dominion Salt, New Zealand
Hydrochloric Acid (HCl)	Herkommer & Bangerte	Not used	Hydrochloric Acid (HCl)	Not applicable
CM Sephadex C-50 or SP Sepharose Big Beads	GE Healthcare	GE Healthcare	Resins for ion exchange	GE Healthcare
Filter cloth (1um)	Wolftechnik Filtersysteme	Wolftechnik Filtersysteme	Ultrafiltration	Koch Membranes
Filter cloth (5um)	Wolftechnik Filtersysteme	Not used	Microfiltration	Tami
GR61PP Membrane	Alfa Laval	Not used		

GE Healthcare

Certificate of Analysis

Product:

SP Sepharose™ Big Beads Food Grade

Code Numbers:
11-0008-29
11-0008-30
11-0008-31

Lot No: 10163437

Test/Characteristic:		Limits:	Results:
1	**Function** Elution volume; ml		
1.1	Wheat Germ Lectin		
	- peak 1	60 – 88	71
	- peak 2	80 – 122	98
	- peak 3	96 – 138	110
1.2	β-Lactoglobulin	147 – 189	157
2	**Total capacity** mmol H^+ / ml packed gel	0.18 – 0.25	0.23
3	**Flow rate at 0.1 MPa**; cm/h	1200 – 1800	1450
4	**Particle size distribution** Volume share within 100 – 300 µm; %	min. 80	98
5	**Microbial contamination** Colony Forming Units / ml suspension	max. 100	0

Manufactured in compliance with our ISO 9001 certified quality management system.

Approval date (Year-Month-Day): 2013-06-03

Expiry date (Year-Month): 2018-05
Manufacturing date (Year-Month): 2013-05

Tests and limits according to AS 45-6015-84 Ed. AB

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Reg.No. SE 55 61 08 1919 01

Quality Assurance
Issued (Year-Month-Day) 2013-06-03 by Sten Pettersson

This document has been electronically produced and is valid without a signature.

28-9653-19 / AC
DOC1103901 / 1
Valid from 2012-02-24

GE Healthcare

SAFETY DATA SHEET

New Zealand

Section 1. Identification

Product name **SP Sepharose™ Big Beads, Food Grade, 10 L**

Catalogue Number 11-0008-30

9011000830

Other means of identification Not available.

Product type Liquid.

Identified uses

Laboratory chemicals Liquid chromatography. Research and Development

Supplier

GE Healthcare UK Ltd
Amersham Place
Little Chalfont
Buckinghamshire HP7 9NA
England
+44 0870 606 1921

GE Healthcare Bio-Sciences
8 Tangihua Street
Auckland 1010

Person who prepared the MSDS :

msdslifesciences@ge.com

Emergency telephone number (with hours of operation)

0800 733 893
(10am - 7pm)

Section 2. Hazards identification

HSNO Classification 3.1 - FLAMMABLE LIQUIDS - Category C
6.4 - EYE IRRITATION - Category A (Irritant)

This material is classified as hazardous according to criteria in the Hazardous Substances (Minimum Degrees of Hazard) Regulations 2001 and has been classified according to the Hazardous Substances (Classifications) Regulations 2001.

This material is classified as a dangerous good according to criteria in New Zealand Standard 5433:2007 Transport of Dangerous Goods on Land.

GHS label elements

Signal word Warning

Hazard statements Flammable liquid and vapor.
Causes serious eye irritation.

Precautionary statements

Prevention Wear protective gloves: 1-4 hours (breakthrough time): butyl rubber, neoprene. Wear eye or face protection: Recommended: safety glasses with side-shields. Keep away from ignition sources such as heat/sparks/open flame. - No smoking. Use explosion-proof electrical, ventilating, lighting and all material-handling equipment. Use only non-sparking tools. Take precautionary measures against static discharge. Keep container tightly closed.

Response IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical advice/attention. Wash hands after handling.

Storage Store in cool/well-ventilated place.

Disposal Dispose of contents and container in accordance with all local, regional, national and international regulations.

Symbol

Other hazards which do not result in classification Not available.

Section 3. Composition/information on ingredients

Substance/mixture Mixture

Other means of identification Not available.

CAS number/other identifiers

CAS number Not applicable.

EC number Mixture.

Product code 11-0008-30

Ingredient name	%	CAS number
Ethanol	14 - 19	64-17-5

There are no additional ingredients present which, within the current knowledge of the supplier and in the concentrations applicable, are classified as hazardous to health or the environment and hence require reporting in this section.

Occupational exposure limits, if available, are listed in Section 8.

Section 4. First aid measures

Description of necessary first aid measures

Inhalation If inhaled, remove to fresh air. Get medical attention if symptoms appear.

Ingestion Do not ingest. Get medical attention if symptoms appear.

Skin contact Wash with soap and water. Get medical attention if irritation develops.

Eye contact Immediately flush eyes with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses. Continue to rinse for at least 10 minutes. Get medical attention.

Most important symptoms/effects, acute and delayed

Potential acute health effects

Inhalation No known significant effects or critical hazards.

Ingestion Irritating to mouth, throat and stomach.

Skin contact No known significant effects or critical hazards.

Eye contact Causes serious eye irritation.

Over-exposure signs/symptoms

Inhalation No specific data.

Ingestion No specific data.

Skin No specific data.

Eyes Adverse symptoms may include the following:
pain or irritation
watering
redness

Indication of immediate medical attention and special treatment needed, if necessary

Specific treatments Not available.

Notes to physician No specific treatment. Treat symptomatically. Contact poison treatment specialist immediately if large quantities have been ingested or inhaled.

Protection of first-aiders No action shall be taken involving any personal risk or without suitable training. It may be dangerous to the person providing aid to give mouth-to-mouth resuscitation.

See toxicological information (section 11)

Section 5. Fire-fighting measures

Extinguishing media

Suitable Use dry chemical, CO_2, water spray (fog) or foam.

Not suitable Do not use water jet.

Specific hazards arising from the chemical Flammable liquid and vapor. In a fire or if heated, a pressure increase will occur and the container may burst, with the risk of a subsequent explosion. Runoff to sewer may create fire or explosion hazard.

Hazardous thermal decomposition products Decomposition products may include the following materials:
carbon dioxide
carbon monoxide

Hazchem code Not available.

Special precautions for fire-fighters	Promptly isolate the scene by removing all persons from the vicinity of the incident if there is a fire. No action shall be taken involving any personal risk or without suitable training. Move containers from fire area if this can be done without risk. Use water spray to keep fire-exposed containers cool.
Special protective equipment for fire-fighters	Fire-fighters should wear appropriate protective equipment and self-contained breathing apparatus (SCBA) with a full face-piece operated in positive pressure mode.

Section 6. Accidental release measures

Personal precautions, protective equipment and emergency procedures	No action shall be taken involving any personal risk or without suitable training. Evacuate surrounding areas. Keep unnecessary and unprotected personnel from entering. Do not touch or walk through spilled material. Shut off all ignition sources. No flares, smoking or flames in hazard area. Avoid breathing vapor or mist. Provide adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Put on appropriate personal protective equipment (see Section 8).
Environmental precautions	Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers. Inform the relevant authorities if the product has caused environmental pollution (sewers, waterways, soil or air).

Methods and materials for containment and cleaning up

Small spill	Stop leak if without risk. Move containers from spill area. Dilute with water and mop up if water-soluble. Alternatively, or if water-insoluble, absorb with an inert dry material and place in an appropriate waste disposal container. Use spark-proof tools and explosion-proof equipment. Dispose of via a licensed waste disposal contractor.
Large spill	Stop leak if without risk. Move containers from spill area. Approach release from upwind. Prevent entry into sewers, water courses, basements or confined areas. Wash spillages into an effluent treatment plant or proceed as follows. Contain and collect spillage with non-combustible, absorbent material e.g. sand, earth, vermiculite or diatomaceous earth and place in container for disposal according to local regulations (see section 13). Use spark-proof tools and explosion-proof equipment. Dispose of via a licensed waste disposal contractor. Contaminated absorbent material may pose the same hazard as the spilled product. Note: see section 1 for emergency contact information and section 13 for waste disposal.

Section 7. Handling and storage

Precautions for safe handling	Put on appropriate personal protective equipment (see Section 8). Eating, drinking and smoking should be prohibited in areas where this material is handled, stored and processed. Workers should wash hands and face before eating, drinking and smoking. Remove contaminated clothing and protective equipment before entering eating areas. Do not ingest. Avoid contact with eyes, skin and clothing. Avoid breathing vapor or mist. Use only with adequate ventilation. Wear appropriate respirator when ventilation is inadequate. Do not enter storage areas and confined spaces unless adequately ventilated. Keep in the original container or an approved alternative made from a compatible material, kept tightly closed when not in use. Store and use away from heat, sparks, open flame or any other ignition source. Use explosion-proof electrical (ventilating, lighting and material handling) equipment. Use only non-sparking tools. Take precautionary measures against electrostatic discharges. To avoid fire or explosion, dissipate static electricity during transfer by grounding and bonding containers and equipment before transferring material. Empty containers retain product residue and can be hazardous. Do not reuse container.
Conditions for safe storage, including any incompatibilities	Store between the following temperatures: 4 to 30°C (39.2 to 86°F). Store in accordance with local regulations. Store in a segregated and approved area. Store in original container protected from direct sunlight in a dry, cool and well-ventilated area, away from incompatible materials (see section 10) and food and drink. Eliminate all ignition sources. Separate from oxidizing materials. Keep container tightly closed and sealed until ready for use. Containers that have been opened must be carefully resealed and kept upright to prevent leakage. Do not store in unlabeled containers. Use appropriate containment to avoid environmental contamination.

Section 8. Exposure controls/personal protection

Control parameters

Occupational exposure limits

Ingredient name	**Exposure limits**
Ethanol	**NZ OSH (New Zealand, 1/2002).** WES-TWA: 1880 mg/m³ 8 hour(s). WES-TWA: 1000 ppm 8 hour(s).

Recommended monitoring procedures	If this product contains ingredients with exposure limits, personal, workplace atmosphere or biological monitoring may be required to determine the effectiveness of the ventilation or other control measures and/or the necessity to use respiratory protective equipment.
Appropriate engineering controls	Use only with adequate ventilation. Use process enclosures, local exhaust ventilation or other engineering controls to keep worker exposure to airborne contaminants below any recommended or statutory limits. The engineering controls also need to keep gas, vapor or dust concentrations below any lower explosive limits. Use explosion-proof ventilation equipment.
Environmental exposure controls	Emissions from ventilation or work process equipment should be checked to ensure they comply with the requirements of environmental protection legislation. In some cases, fume scrubbers, filters or engineering modifications to the process equipment will be necessary to reduce emissions to acceptable levels.

Individual protection measures

Hygiene measures	Wash hands, forearms and face thoroughly after handling chemical products, before eating, smoking and using the lavatory and at the end of the working period. Appropriate techniques should be used to remove potentially contaminated clothing. Wash contaminated clothing before reusing. Ensure that eyewash stations and safety showers are close to the workstation location.
Respiratory protection	Use a properly fitted, air-purifying or air-fed respirator complying with an approved standard if a risk assessment indicates this is necessary. Respirator selection must be based on known or anticipated exposure levels, the hazards of the product and the safe working limits of the selected respirator. Recommended: A respirator is not needed under normal and intended conditions of product use.
Hand protection	1-4 hours (breakthrough time): butyl rubber, neoprene
Eye protection	Safety eyewear complying with an approved standard should be used when a risk assessment indicates this is necessary to avoid exposure to liquid splashes, mists, gases or dusts. Recommended: safety glasses with side-shields
Skin protection	Personal protective equipment for the body should be selected based on the task being performed and the risks involved and should be approved by a specialist before handling this product. Recommended: lab coat

Section 9. Physical and chemical properties

Appearance	
Physical state	Liquid. [and Suspension.]
Color	solution : Colorless. / Suspension. : White.
Odor	Sweetish. Alcohol-like. [Slight]
Odor threshold	180 ppm
pH	Not available.
Melting point	Not available.
Boiling point	Not available.
Flash point	Closed cup: 38 to 43°C (100.4 to 109.4°F)
Burning rate	Not applicable.
Burning time	Not applicable.
Evaporation rate	Not available.
Flammability (solid, gas)	Not available.
Lower and upper explosive (flammable) limits	Not available.
Vapor pressure	Not available.
Vapor density	Not available.
Relative density	Not available.
Solubility	Easily soluble in the following materials: cold water and hot water.
Partition coefficient: n-octanol/water	Not available.
Auto-ignition temperature	Not available.
Decomposition temperature	Not available.
SADT	Not available.
Viscosity	Not available.
Aerosol product	
Type of aerosol	Not applicable.
Heat of combustion	Not available.
Ignition distance	Not applicable.
Enclosed space ignition - Time equivalent	Not applicable.
Enclosed space ignition - Deflagration density	Not applicable.
Flame height	Not applicable.
Flame duration	Not applicable.

Section 10. Stability and reactivity

Chemical stability The product is stable.

Possibility of hazardous reactions Under normal conditions of storage and use, hazardous reactions will not occur.

Conditions to avoid Avoid all possible sources of ignition (spark or flame). Do not pressurize, cut, weld, braze, solder, drill, grind or expose containers to heat or sources of ignition.

Incompatible materials Reactive or incompatible with the following materials:
oxidizing materials

Hazardous decomposition products Under normal conditions of storage and use, hazardous decomposition products should not be produced.

Section 11. Toxicological information

Information on the likely routes of exposure

Inhalation No known significant effects or critical hazards.

Ingestion Irritating to mouth, throat and stomach.

Skin contact No known significant effects or critical hazards.

Eye contact Causes serious eye irritation.

Symptoms related to the physical, chemical and toxicological characteristics

Inhalation No specific data.

Ingestion No specific data.

Skin contact No specific data.

Eye contact Adverse symptoms may include the following:
pain or irritation
watering
redness

Delayed and immediate effects and also chronic effects from short and long term exposure

Acute toxicity

Product/ingredient name	Result	Species	Dose	Exposure
Ethanol	LC50 Inhalation Vapor	Rat	124700 mg/m3	4 hours
	LD50 Oral	Rat	7 g/kg	-

Irritation/Corrosion

Product/ingredient name	Result	Species	Score	Exposure	Observation
Ethanol	Eyes - Mild irritant	Rabbit	-	-	-
	Eyes - Moderate irritant	Rabbit	-	-	-
	Eyes - Severe irritant	Rabbit	-	-	-
	Skin - Mild irritant	Rabbit	-	-	-
	Skin - Moderate irritant	Rabbit	-	-	-

Conclusion/Summary

Skin Repeated exposure may cause skin dryness or cracking.

Sensitization

Not available.

Potential chronic health effects

General No known significant effects or critical hazards.

Inhalation No known significant effects or critical hazards.

Ingestion No known significant effects or critical hazards.

Skin contact No known significant effects or critical hazards.

Eye contact No known significant effects or critical hazards.

Carcinogenicity No known significant effects or critical hazards.

Mutagenicity No known significant effects or critical hazards.

Teratogenicity No known significant effects or critical hazards.

Developmental effects No known significant effects or critical hazards.

Fertility effects No known significant effects or critical hazards.

Chronic toxicity

Not available.

Carcinogenicity

Not available.

Mutagenicity

Not available.

Teratogenicity

Not available.

Reproductive toxicity

Not available.

Specific target organ toxicity

Not available.

Aspiration hazard

Not available.

Numerical measures of toxicity

Acute toxicity estimates

Not available.

Other information

Adverse symptoms include the following: kidney abnormalities, liver abnormalities
Adverse symptoms may include the following: central nervous system depression

Section 12. Ecological information

Ecotoxicity No known significant effects or critical hazards.

Aquatic and terrestrial toxicity

Product/ingredient name	Result	Species	Exposure
Ethanol	Acute EC50 2000 ug/L Fresh water	Daphnia - Daphnia magna	48 hours
	Acute LC50 25500 ug/L Marine water	Crustaceans - Artemia franchiscana - LARVAE	48 hours
	Acute LC50 42000 ug/L Fresh water	Fish - Oncorhynchus mykiss	4 days
	Chronic NOEC <6.3 g/L Fresh water	Daphnia - Daphnia magna	48 hours

Persistence/degradability

Product/ingredient name	Test	Result	Dose	Inoculum
Ethanol	-	100 % - Readily - 20 days	-	-

Product/ingredient name	Aquatic half-life	Photolysis	Biodegradability
Ethanol	-	-	Readily

Bioaccumulative potential

Product/ingredient name	$LogP_{ow}$	BCF	Potential
Ethanol	-	0.66	low

Mobility in soil

Soil/water partition coefficient (K_{OC}) Not available.

Other adverse effects No known significant effects or critical hazards.

Section 13. Disposal considerations

Disposal methods The generation of waste should be avoided or minimized wherever possible. Empty containers or liners may retain some product residues. This material and its container must be disposed of in a safe way. Significant quantities of waste product residues should not be disposed of via the foul sewer but processed in a suitable effluent treatment plant. Dispose of surplus and non-recyclable products via a licensed waste disposal contractor. Disposal of this product, solutions and any by-products should at all times comply with the requirements of environmental protection and waste disposal legislation and any regional local authority requirements. Avoid dispersal of spilled material and runoff and contact with soil, waterways, drains and sewers.

Section 14. Transport information

Regulatory information	UN number	Proper shipping name	Classes	PG*
New Zealand Class	Not regulated.	-	-	-
ADG Class	Not regulated.	-	-	-
UN Class	Not regulated.	-	-	-
ADR/RID Class	Not regulated.	-	-	-
IATA Class	Not regulated.	-	-	-
		Remarks IATA Special Provision A 58 - Aqueous solutions containing 24% or less alcohol by volume is not subject to these regulations.		
IMDG Class	Not regulated.	-	-	-

PG* : Packing group

Section 15. Regulatory information

New Zealand Inventory of Chemicals (NZIoC) All components are listed or exempted.

HSNO Approval Number HSR001144

HSNO Group Standard Not available.

HSNO Classification 3.1 - FLAMMABLE LIQUIDS - Category C
6.4 - EYE IRRITATION - Category A (Irritant)

Australia inventory (AICS) All components are listed or exempted.

Safety, health and environmental regulations specific for the product No known specific national and/or regional regulations applicable to this product (including its ingredients).

Section 16. Other information

History

Date of printing 12/16/2010.

Date of issue/ Date of revision 15 December 2010

Date of previous issue No previous validation.

Version 0.9

Key to abbreviations ADN/ADNR = European Provisions concerning the International Carriage of Dangerous Goods by Inland Waterway
ADR = The European Agreement concerning the International Carriage of Dangerous Goods by Road
ATE = Acute Toxicity Estimate
BCF = Bioconcentration Factor
GHS = Globally Harmonized System of Classification and Labelling of Chemicals
IATA = International Air Transport Association
IBC = Intermediate Bulk Container
IMDG = International Maritime Dangerous Goods
LogPow = logarithm of the octanol/water partition coefficient
MARPOL 73/78 = International Convention for the Prevention of Pollution From Ships, 1973 as modified by the Protocol of 1978. ("Marpol" = marine pollution)
RID = The Regulations concerning the International Carriage of Dangerous Goods by Rail
UN = United Nations

References Not available.

Indicates information that has changed from previously issued version.

Notice to reader

To the best of our knowledge, the information contained herein is accurate. However, neither the above-named supplier, nor any of its subsidiaries, assumes any liability whatsoever for the accuracy or completeness of the information contained herein.
Final determination of suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards that exist.

Customer Specification Sheet

Synlait Lactoferrin 5kg Reclosable Pouch PPRI01005

8 December 2015

Issue Number: 01

Amcor Item:

Customer Item Code:

Customer	Synlait Milk Ltd
Description	SYN LACTOFERRIN 5KG
Material Structure description	Coated Polyester(14um)/ ink/adhesive/Foil(7um)/Nylon(15um) Polyethylene (90um)
Yield:	148.6gsm* Tolerance: +/-10gsm
Gauge:	133µm* Tolerance: +/-10µm
Estimated Oxygen Transmission Rate:	<0.3 cc/m^2/24hrs(100% O_2) 23°C/ 0% RH
Estimated Water Vapour Transmission Rate:	<0.3 g/m^2/24hrs 38°C 90% RH

* Excludes zipper

Amcor Flexibles Asia Pacific - ANZ
74 Branston Street; Hornby; Christchurch 8042; New Zealand
Ph: +64 3 349 1250 www.amcor.com

Customer Specification Sheet

Product and Packing Specifications:

Printing Process:	Flexographic.
Colour and Coatings:	To match customer approved standard.
Identification Labels:	Cartons: labels to state ID number, Item number, Description, Customer Code, Quantity, Carton number, Date and packer Pallet: Customer, product description, quantity, customer order number, customer stock number, pallet number, date, number of rolls, and Amcor job number.
Carton Handling:	Pouches should be kept out of direct natural light/sunlight and in a well-ventilated area. It is advantageous to condition the cartons to packing room temperature at least 24 hrs prior to use. At all times when not in use the carton should be sealed so performance is not impaired or contamination permitted.

Specification Data:

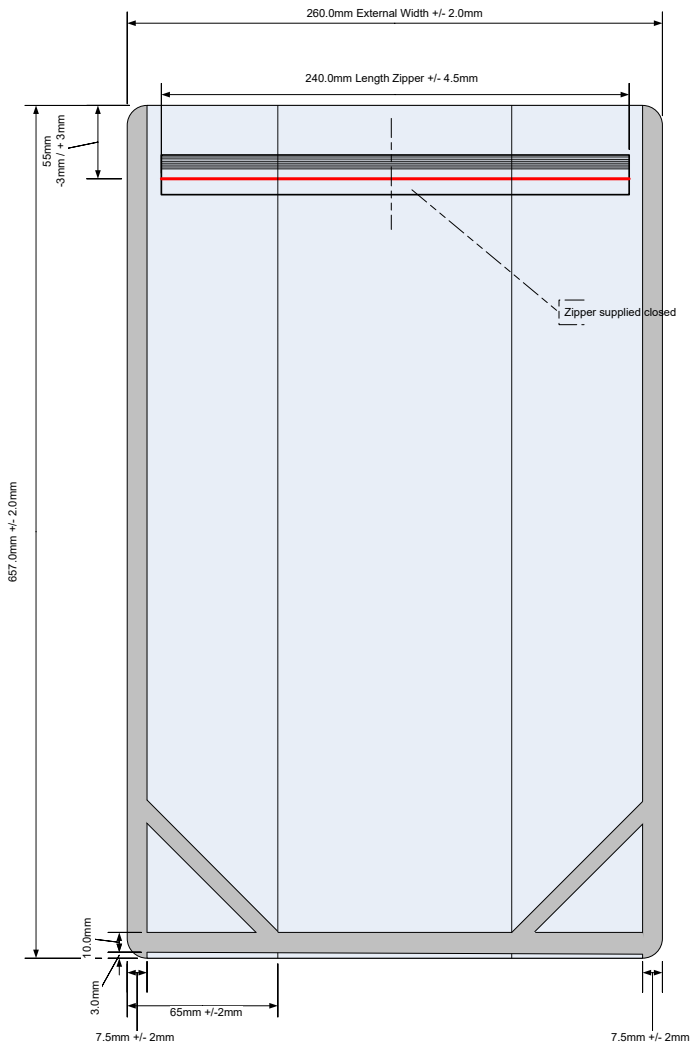
Customer Item Number	Amcor Item Number	Description		Length	Bags per Bundle	Bags per Carton
PPRI01005	1044979	SYN LACTOFERRIN 5KG	260X130X660 L81 RQPH	657	25	150

Reason for Revision:

Design change to 1 colour.

Customer Specification Sheet

Material Diagram: (not to scale)



Approved by (Amcor):		Approved by (Customer):
Position:	Quality Manager	Position:
Date:	08/12/2015	Date:

Amcor Flexibles Asia Pacific - ANZ
74 Branston Street; Hornby; Christchurch 8042; New Zealand
Ph: +64 3 349 1250 www.amcor.com

Sensory Attributes

Parameter	Description	Test method
Appearance	pink to tan, free flowing powder	Visual Observation

Microbiological Standards

Parameter	Unit	Max.	Test method
Aerobic Plate Count	cfu/g	1000	ISO 4833:2003
E.coli	/g	Not detected	ISO 11866 /IDF 170-1
Yeast and moulds	cfu/g	10	ISO 6611/IDF 94:2004
Salmonella	/250g	Not detected	ISO 6579:2002 (E)
Coagulase Positive Staphylococcus	/g	Not detected	ISO 6888-3:2003
Coliform	/g	Not detected	ISO 11866 /IDF 170-1
E.sakazaki	/300g	Not detected	ISO/TS 22964 / IDF/RM 210:2006
Enterobacteriaceae	/g	Not detected	ISO 21528-1:2004

Contaminants and Residues

Parameter	Unit	Limit	Test method
Nitrates	mg/kg	≤50	NZJDST 15, 83-90, 1980, ISO 14673-2, IDF 189-2, AOAC 968.07 (mod)
Nitrites	mg/kg	≤2	NZJDST 15, 83-90, 1980, ISO 14673-2, IDF 189-2, AOAC 968.07 (mod)
Heavy Metals	mg/kg	<10	Acid Digest ICPMS
Melamine [1]	ppm	<0.1	LC-MS/MS **(Detectable limit)**
Arsenic [1]	mg/kg	<0.02	Wet oxidation ICP MS **(Detectable Limit)**
Aluminium	mg/kg	<4.8	Wet oxidation ICP-MS
Cadmium	mg/kg	<0.1	Wet oxidation ICP-MS
Mercury	mg/kg	<0.1	Acid Digest ICPMS
Lead	mg/kg	<0.15	Wet oxidation ICP MS
Aflatoxin M1	µg/kg	<0.5	G Barbieri et al, J Food Sci, 59 (1994) p1313-

[1] to be reported as "Not Detected" on the COA

Product Statements

This product complies with the following requirements:

General spec	Spec descriptions
	HALAL
	GMO-free

This product is manufactured and packed according to Synlait RMP requirements

Synlait Milk Ltd
1028 Heslerton Road
RD13, Rakaia 7783
New Zealand
P +64 3 373 3000
www.synlait.com

Instructions for use

Food contact substance notification

SP Sepharose Big Beads, Food Grade (CAS Reg. No. 676618-71-6) is approved by the U.S. Food and Drug Administration (FDA) to be used as a food contact substance according to notification FCN 000 443.

Further information on the FDA premarket notification program for food contact substances is available on the agency's internet site.

Intended use

The ion exchange chromatography medium, SP Sepharose Big Beads, Food Grade, is intended to be used for the separation of proteins or other compounds present in similar concentrations from liquid foods such as milk, whey, fruit juices, beer, and wine.

Pre-use washing procedure

After packing into the column and before being used the first time, the medium should be washed as follows.

Step 1: 5 column volumes water

Step 2: 5 column volumes 1M NaCl

Step 3: Leave in 1M NaCl for 12 h

Step 4: 5 column volumes water

Process conditions and limitations

The chromatography medium is sensitive to hydrolysis at extreme pH, particularly on the acidic side. In order to avoid excessive degradation the exposure time at low pH should be limited. For continuous use, the process conditions should be between pH 4.5 and 12 and temperatures below 40°C. Use for limited time is also possible at lower pH as follows: At pH 4, the maximum exposure time is 20 000 h at 20°C and 4000 h at 40°C over the lifetime of the medium. At pH 3, the maximum exposure time is 7500 h at 20°C and 1700 h at 40°C over the lifetime of the medium. Cleaning may take place at up to pH 14 when performed at 20°C and when performed at pH 13.4 up to a temperature of 60°C.

Ordering information

Product	Pack size	Code No.
SP Sepharose Big Beads Food Grade	1L	11-0008-29
SP Sepharose Big Beads Food Grade	10L	11-0008-30

GE Healthcare Bio-Sciences AB
Björkgatan 30
751 84 Uppsala
Sweden

11-0026-62 AB 05/2009

imagination at work

PART 7:

APPENDIX 2: Synlait Manufacturing Certification And Registration Certificates

The data and information presented within Appendix 2 is **generally available**.

PART 7:
APPENDIX 3: Analytical Methodology, Specifications And Results

The data and information presented within Appendix 3 is **generally available**.

PART 7:
APPENDIX 4: International Regulations

The information presented within Appendix 4 is **generally available**.

PART 7:
APPENDIX 5: Synlait Manufactured Product Examples

The data and information presented within Appendix 5 is **generally available**.

光明乳业股份有限公司乳业研究院
地址:上海市江场西路 1518 号 2 号楼
电话:(021)66553119
传真:(021)66553708
邮编:200436
Http: // skldb.brightdairy.com

Supporting letter on the use of bovine lactoferrin in infant formula

In a recently completed clinical trial (NCT02239588) evaluating the effects of an infant formula (0-6months) manufactured by Synlait Milk, containing bovine lactoferrin at 60mg/100g, normal growth and development was observed and the formula well tolerated

(Name): 苏米亚

(Signature): (b) (4)

(Date): 2016.8.1

光明乳业
BRIGHT DAIRY

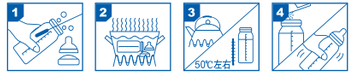
- **PURE CANTERBURY** Infant Formula Milk Powder is processed according to the standards of the Codex Alimentarius Commission (CAC) and the "*Chinese Dietary Reference Intakes*" (*Chinese DRIs*).It is made in accordance with the nutritional and dietary needs of babies, and gives babies the required nutritional support.
- **培儿贝瑞**婴儿配方奶粉参考国际食品法典委员会(CAC)的标准以及《中国居民膳食营养素参考摄入量》，针对宝宝膳食结构特点，为宝宝提供多方面的营养支持。

Important Notice/注意事项

冲调前请洗净双手，并保持手部干爽，以免水滴带入导致奶粉受潮、结团。对于0-6月的婴儿最理想的食品是母乳，在母乳不足或无母乳时可食用本产品。调奶时请用专用量匙，按喂哺建议量冲调，未经医生建议，请勿擅自改变冲调比例，否则可能损害宝宝的健康。

Instructions for Use/冲调方法

1.清洗奶瓶、奶嘴、瓶盖；2.沸水中煮五分钟；3.饮用水煮沸后冷却至50°C，将正确水量倒入消毒后的奶瓶；4.使用专用量匙，参照喂哺表加入正确分量奶粉，盖紧瓶盖后摇动使之充分溶解，待冷却至适宜温度后即可喂哺。



产品类别及属性：乳基粉状婴儿配方食品

原产国：新西兰

注册编号：540
企业名称：Synlait Milk Limited
注册地址：1028 Heslerton Road, Rakaia, Canterbury, New Zealand
电话：+64 3 373 3000

中国总经销商：光明乳业股份有限公司
地址：上海市吴中路578号

9 421028 300124

培儿贝瑞
国际母婴中国服务中心
400 700 1717

PPRI00330

原装原罐进口

PURE CANTERBURY
PURE ECO · HIGH QUALITY
NEW ZEALAND

PURE™ CANTERBURY 培儿贝瑞

——新西兰坎特伯雷平原——

Milk is collected from farm and spray dried within 24 hours
牛奶24小时内浓缩干燥成粉

The Canterbury region is located in the South Island of New Zealand. Pure air, and natural water coming from the snow capped Southern Alps. Cows graze on fresh grass. This young country with its pure ecological environment has created the Pure Canterbury.

雪山牧场，鲜嫩的牧草，清新的空气……是新西兰为之骄傲的自然环境。这片年轻、充满生机的土地缔造了**培儿贝瑞**的纯净品质。

同时邀请您登陆网站**www.4007001717.com.cn**，感受纯净**培儿贝瑞**。

Ingredients/配料

Ingredients: Skim milk, Whole milk, Lactose, Refined vegetable oils (Soya bean oil, Coconut oil, Sunflowerseed oil, Rapeseed oil), Demineralized whey powder, Whey protein concentrate, 1,3-Dioleoyl 2-palmitoyl Triglyceride, Polyfructose, Galacto-oligosaccharide, ARA(Arachidonic acid oil), DHA(Docosahexaenoic acid oil), Minerals (Potassium chloride, Sodium citrate, Magnesium chloride, Calcium carbonate, Ferrous gluconate, Zinc sulfate, Copper gluconate, Manganese sulfate, Potassium iodide, Sodium selenite), Vitamins(L-Ascorbic acid, Choline chloride, dl-α-Tocopherol acetate, Calcium D-Pantothenate,Vitamin A Acetate, Nicotinamide, Vitamin D_3, Cyanocobalamin, Phytonadione, Thiamine hydrochloride, Riboflavin, Pyridoxine hydrochloride, Folic acid, D-Biotin), Taurine, Nucleotides (Guanosine 5' Monophosphate Disodium, Inosine 5' Monophosphate Disodium, Uridine 5' Monophosphate Disodium, Adenosine 5' Monophosphate, Cytidine 5' Monophosphate), Lactoferrin, Citric acid, Calcium hydroxide, Ascorbyl palmitate.

配料：脱脂牛奶、全脂牛奶、乳糖、精炼植物油(大豆油、椰子油、葵花籽油、菜籽油)、脱盐乳清粉、浓缩乳清蛋白粉、1，3-二油酸 2-棕榈酸甘油三酯、多聚果糖、低聚半乳糖、ARA(花生四烯酸油脂)、DHA(二十二碳六烯酸油脂)、矿物质(氯化钾、柠檬酸钠、氯化镁、碳酸钙、葡萄糖酸亚铁、硫酸锌、葡萄糖酸铜、硫酸锰、碘化钾、亚硒酸钠)、维生素(L-抗坏血酸、氯化胆碱、dl-α-醋酸生育酚、D-泛酸钙、醋酸维生素A、烟酰胺、维生素D_3、氰钴胺、植物甲萘醌、盐酸硫胺素、核黄素、盐酸吡哆醇、叶酸、D-生物素)、牛磺酸、核苷酸(5'-鸟苷酸二钠、5'-肌苷酸二钠、5'-尿苷酸二钠、5'单磷酸腺苷、5'单磷酸胞苷)、乳铁蛋白、柠檬酸、氢氧化钙、抗坏血酸棕榈酸酯。

Suggested Feeding Table/喂哺用量建议表

1平匙奶粉约等于7.5克冲50mL水

婴儿年龄	温开水量(毫升)	量匙数/次	喂哺次数/天
0-2 weeks(周)	50	1	7-9
2-4 weeks(周)	100	2	6-8
1-2 months(月)	150	3	4-6
2-3 months(月)	150	3	5-6
3-6 months(月)	200	4	4-5

*喂哺用量建议表是根据平均的需要量制定的。

Storage Conditions/贮存条件

产品应存放于阴凉干燥处，常温保存(室温20-25°C)，以免遇高温后影响产品品质。开罐后请务必盖紧塑料盖，并请于四周内食用完毕。

生产日期MFD(YYYY/MM/DD)、保质期至USE BY(YYYY/MM/DD)及产品批号(LOT)请见罐底所示。请在保质期前食用。

NEW ZEALAND MADE

Nutrition Information/营养成分表

Nutrients 营养成分	Unit 单位	Average content/100g 每100克(g)平均含量	Average content/100kJ 每100千焦(kJ)平均含量
能量 (Energy)	kJ	2096	273kJ/100mL
蛋白质 (Protein)	g	11.5	0.55
乳铁蛋白 (Lactoferrin)	mg	30	1.4
脂肪 (Fat)	g	25.9	1.24
1,3-二油酸 2-棕榈酸甘油三酯 1,3-Dioleoyl 2-palmitoyl Triglyceride	g	3.3	0.16
亚油酸 (Linoleic acid)	g	4.16	0.20
α-亚麻酸 (α-Linolenic acid)	mg	310	15
二十二碳六烯酸 (DHA)	mg	50	2.4
二十碳四烯酸 (ARA)	mg	80	3.8
碳水化合物 (Carbohydrate)	g	54.2	2.6
多聚果糖 (Polyfructose)	mg	2000	95.4
低聚半乳糖 (GOS)	mg	400	19.1
牛磺酸 (Taurine)	mg	44	2
核苷酸 (Nucleotides)	mg	23.5	1.1
维生素			
维生素A (Vitamin A)	μgRE	500	24
维生素D (Vitamin D)	μg	9.0	0.43
维生素E (Vitamin E)	mgα-TE	11.4	0.54
维生素K_1 (Vitamin K_1)	μg	40.5	1.9
维生素B_1 (Vitamin B_1)	μg	786	38
维生素B_2 (Vitamin B_2)	μg	1420	68
维生素B_6 (Vitamin B_6)	μg	434	20.7
维生素B_{12} (Vitamin B_{12})	μg	1.80	0.09
烟酸 (Niacin)	μg	4800	229
叶酸 (Folic acid)	μg	145	6.9
泛酸 (Pantothenic acid)	μg	5800	277
维生素C (Vitamin C)	mg	180	8.6
生物素 (Biotin)	μg	20	1.0
胆碱 (Choline)	mg	115	5.5
矿物质			
钠 (Sodium)	mg	130	6
钾 (Potassium)	mg	545	26
铜 (Copper)	μg	328	15.6
镁 (Magnesium)	mg	48	2.3
铁 (Iron)	mg	5.0	0.24
锌 (Zinc)	mg	5.2	0.25
锰 (Manganese)	μg	101	4.8
钙 (Calcium)	mg	350	17
磷 (Phosphorus)	mg	200	10
碘 (Iodine)	μg	93	4.4
氯 (Chloride)	mg	359	17
硒 (Selenium)	μg	15	0.72

803794

YELLOW MAGENTA CYAN BLACK A2 YELLOW A2 BROWN BLUE

INGREDIENTS/配料: 乳固体(乳糖、脱盐乳清粉、乳清蛋白粉)，植物油，全脂牛奶，低脂半乳糖，脱脂牛奶，矿物质(柠檬酸钠、磷酸氢钙、氯化钾、碳酸钙、氯化镁、磷酸氢二钾、硫酸亚铁、硫酸锌、亚硒酸钠、硫酸铜、硫酸锰、碘化钾)，花生四烯酸油脂，金枪鱼油，维生素(L-抗坏血酸、氯化胆碱、dl-α-醋酸生育酚、肌醇、醋酸维生素A、烟酰胺、D-泛酸钙、维生素D₃、植物甲萘醌、盐酸硫胺素、盐酸吡哆醇、氰钴胺、核黄素、叶酸、D-生物素)，氯氧化钙，牛磺酸，乳铁蛋白，核苷酸(5'单磷酸胞苷、5'-尿苷酸二钠、5'单磷酸腺苷、5'-肌苷酸二钠、5'-鸟苷酸二钠)，柠檬酸，左旋肉碱。

ALLERGY CAUTION/过敏提示: 本产品含有大豆、鱼油、牛奶成分。

STORAGE CONDITIONS/贮存条件: 如果罐装铝箔封口损坏或缺失请勿使用。请检查罐底的奶粉有效期。请贮存在阴凉干燥的地方。每次开罐使用后务必重新盖紧塑料盖。开罐后应在4个星期内用完。听装规格均按重量计算(而非按容量计算)。

IMPORTANT NOTICE/重要信息: 对于0~6月的婴儿最理想的食品是母乳，在母乳不足或无母乳时可食用本产品。

WARNING/警告: 严格按说明操作。请按要求准备奶瓶和奶嘴。除非医生另有建议，否则请勿改变奶粉的冲调比例。不正确的冲调方法可能会严重危及宝宝健康。

PRODUCT TYPE/产品类别及属性: 乳基婴儿配方奶粉。

MANUFACTURE DATE/生产日期:
(年/月/日), 保质期至(年/月/日),
生产批号见罐底。

原产国: 新西兰
出品商: A2 Infant Nutrition Ltd
生产商: Synlait Milk Limited
地址: 1028 Heslerton Road,
Rakaia,Canterbury,
New Zealand
生产商注册编号: 540

进口商: 中国农垦控股上海公司
地址: 上海市浦东新区浦东大道2123号3层E区1820－1821室
邮编: 200135

客服热线: 4008204056
www.a2nutrition.cn
PPRI00160

POSITION ONLY 100%
9 421902 960000

营养成分表 NUTRITION INFORMATION 营养素/Nutrients	单位 Unit	平均含量/Average Quantity 每100克奶粉 Per 100g	每100千焦 Per 100kJ
能量/energy	kJ	2103	100
蛋白质/protein	g	10.7	0.51
- 乳清蛋白/whey protein	g	6.42	0.31
- 酪蛋白/casein protein	g	4.28	0.20
脂肪/fat	g	26.0	1.24
- 亚油酸/linoleic acid	g	4.20	0.20
- α-亚麻酸/α-linolenic acid (ALA)	mg	450	21.4
亚油酸与α-亚麻酸(ALA)比值		9.3:1	9.3:1
- 二十二碳六烯酸/ docosahexaenoic acid (DHA)	mg	90.0	4.28
二十二碳六烯酸/ docosahexaenoic acid (DHA)	%总脂肪酸	0.37	0.37
- 二十碳四烯酸/arachidonic acid (ARA)	mg	140	6.66
二十碳四烯酸/arachidonic acid (ARA)	%总脂肪酸	0.57	0.57
碳水化合物/carbohydrate	g	54.9	2.61
- 乳糖/lactose	g	52.0	2.47
低聚半乳糖/ galacto-oligosaccharides (GOS)	g	3.00	0.14
维生素 A/vitamin A	μg RE	510	24.3
维生素 D/vitamin D	μg	6.90	0.33
维生素 E/vitamin E	mg α-TE	7.50	0.36
维生素 K_1/vitamin K_1	μg	46.0	2.19
维生素 B_1/vitamin B_1	μg	550	26.2
维生素 B_2/vitamin B_2	μg	1010	48.0
维生素 B_6/vitamin B_6	μg	415	19.7
维生素 B_{12}/ vitamin B_{12}	μg	2.00	0.10
烟酸/niacin	μg	3700	176
叶酸/folic acid	μg	75.0	3.57
泛酸/pantothenic acid	μg	3500	166
维生素 C /vitamin C	mg	145	6.90
生物素/biotin	μg	22.5	1.07
胆碱/choline	mg	94.0	4.47
肌醇/inositol	mg	32.7	1.56
钠/sodium	mg	165	7.85
钾/potassium	mg	540	25.7
铜/copper	μg	365	17.4
镁/magnesium	mg	48.0	2.28
铁/iron	mg	5.50	0.26
锌/zinc	mg	5.10	0.24
锰/manganese	μg	320	15.2
钙/calcium	mg	390	18.5
磷/phosphorus	mg	260	12.4
钙磷比值/Ca:P		1.5:1	1.5:1
碘/iodine	μg	70.0	3.33
氯/chlorine	mg	340	16.2
硒/selenium	μg	18.3	0.87
牛磺酸/taurine	mg	39.0	1.85
左旋肉碱/l-carnitine	mg	8.50	0.40
核苷酸/nucleotides	mg	25.0	1.19
乳铁蛋白/lactoferrin	mg	30.0	1.43

The a2 Milk Company™

PROUDLY MADE IN NEW ZEALAND 新西兰原产原装全进口

a2 PLATINUM® 白金™

婴儿配方奶粉

升级配方[1]

a2™ 源乳™配方

专利应用的A2奶牛基因检测[2]

- ✓ TRUE a2™品质保证
- ✓ 含有DHA
- ✓ 含有膳食纤维(低聚半乳糖)

1 2 3

婴儿配方奶粉
0-6个月婴儿

净含量: 900克

- ✓ a2™ Natural Sourced Milk
  a2™ 源乳™ 配方
- ✓ Patented use of bovine genotype testing for A2 beta-casein
  专利应用的A2 β-酪蛋白奶牛基因检测[2]
- ✓ TRUE a2™ quality assurance
  TRUE a2™ 品质保证

Preparation Instructions 冲调方法

1. 冲调奶粉前要洗手，煮沸或使用灭菌器对所有喂食用具进行消毒。
2. 煮沸饮用水，晾至适温，酌量将水注入经消毒的奶瓶中，晾至温热喂食宝宝。
3. 仅使用罐中配备的量勺。轻轻装满量勺，并用罐口的刮平器刮平。不要挤压奶粉。
4. 每50毫升水加一平勺奶粉。盖上瓶盖轻快地摇晃以加速其溶解。
5. 在手腕上测试温度是否合适。冲调好奶粉后要立即喂食，没有吃完的要倒掉。

奶粉按需冲调。
冲调完毕后应尽快喂食。

a2 PLATINUM® Premium Infant & Growing Up Milk formulas are made and packed in New Zealand, using strict quality and safety practices, it's the only one that combines age-appropriate key ingredients with patented properties of A2 beta-casein. This means that a2 PLATINUM® Premium Infant & Growing Up Milk formulas provide your baby with advanced tailored nutrition you can trust.

a2 PLATINUM® 白金™ 系列婴幼儿配方奶粉新西兰原产原装全进口，执行严格的品质与安全标准。独特的产品配方臻选了专利A2 β-酪蛋白[3]，同时针对婴幼儿不同生长阶段的营养需求添加了各种营养成分。
a2 PLATINUM® 白金™ 系列婴幼儿配方奶粉给予宝宝全面营养，值得信赖。

1 a2 PLATINUM® 白金™ 婴儿配方奶粉

Specially formulated for babies from birth to 6 months old. It is nutritionally complete, providing key ingredients essential for growth and development. The exclusive formulation is based on patented properties of A2 beta-casein and patented use of bovine genotype testing for A2 beta-casein.
本品适用于0-6个月的宝宝。本产品营养全面，提供了婴儿生长发育所需的各种营养成分。独特的产品基于专利A2 β-酪蛋白[3]及专利应用的奶牛基因检测技术[2]。

FEEDING GUIDE / 喂哺指导

Age of Baby 婴儿年龄	Cooled Boiled Water (mL) 温开水量(毫升)	Level Scoops* 奶粉(勺)	Formula Feeds Per Day 每日喂哺次数
0-2 weeks (周)	50	1	7-9
2-8 weeks (周)	100	2	5-6
2-4 months (月)	150	3	5-6
4-6 months (月)	200	4	4-5

*1量勺奶粉≈7.5g
请注意: 每50毫升水加一平勺奶粉，冲调约56毫升的配方奶。本喂哺指导只是一般的指引。在最初的几个星期，新生儿可能无法完成一个完整喂哺量。没有吃完的奶要倒掉。

a2 Milk®, a2 Platinum®, The a2 Milk Company™是a2牛奶公司的注册商标。

参考资料:
1. 和原配方相比
2. 专利号: ZL 0381 7 445.3
3. 专利号: ZL 2003 8 0104926.5

803794

CLEAR BASE COAT & VARNISH LIMIT
L: 391.00mm x H: 162.00mm

BASE COLOUR LIMIT (MAXIMUM PRINT AREA)
L: 393.00mm x H: 160.00mm

MAXIMUM TEXT LIMIT
L: 393.00mm x H: 149.00mm

BARCODE LIMIT
L: 70.00mm x H: 50.00mm

803760

GOLD WHITE SHARP YELLOW MAGENTA CYAN PURPLE DK BLUE BLACK

产品类别及属性

粉状乳基婴儿配方食品

配料表

脱盐乳清粉，植物油，乳糖，1,3-二油酸 2-棕榈酸甘油三酯（结构脂OPO），脱脂牛奶，全脂牛奶，膳食纤维（低聚半乳糖，低聚果糖，多聚果糖），乳清蛋白粉，矿物质（柠檬酸钠，磷酸氢二钾，氯化钾，硫酸铜，氯化镁，硫酸亚铁，硫酸锌，硫酸锰，碳酸钙，磷酸三钙，碘化钾，亚硒酸钠），维生素（醋酸维生素A，维生素D_3，dl-α-醋酸生育酚，植物甲萘醌，盐酸硫胺素，核黄素，盐酸吡哆醇，氰钴胺，烟酰胺，叶酸，D-泛酸钙，L-抗坏血酸钠，D-生物素，氯化胆碱，肌醇），核苷酸（5′单磷酸胞苷，5′-尿苷酸二钠，5′单磷酸腺苷，5′-肌苷酸二钠，5′-鸟苷酸二钠），牛磺酸，氢氧化钙，柠檬酸，花生四烯酸油脂（来源：高山被孢霉），二十二碳六烯酸油脂（来源：金枪鱼油），乳铁蛋白。

贮存条件

请将本品放置在阴凉干燥处保存。在罐底注明的保质日期前使用。开封后盖紧罐盖密封保存，勿放冰箱，并于4周内食用完毕。如本品密封金属箔破损，请勿食用。若仅罐体轻微变形，罐体依然密封良好，仍可以食用。

喂哺指导

婴儿年龄	建议每次喂哺量 温开水用量	奶粉量勺数	建议每日喂哺次数
0-2周	50mL	1	7-9
2周-2个月	100mL	2	5-6
2-4个月	150mL	3	5-6
4-6个月	200mL	4	4-5

- 1量勺奶粉 ~ 7.5 克
- 冲调比例：每50毫升的温水加入1量勺奶粉（大约得到56毫升奶液）。
- 此喂哺指导仅为通用指导，您的宝宝可能需要少于或者多于建议的奶液。

重要声明

对于0-6月的婴儿最理想的食品是母乳。在母乳不足或无母乳时可食用本产品。使用前请先向您的医生或健康顾问咨询。

注意事项

冲调好的配方奶请在1小时内用完，未用完的配方奶必须倒掉。严格遵循冲调指南及喂哺指导中的冲调比例进行冲调。未经医嘱，不得改变冲调比例。不恰当的冲调和使用可能会严重影响宝宝的生长发育及健康。

营养成分表

项目	单位	每100g 平均含	每100kJ 平均含	每100mL 标准冲调液 平均含
能量Energy	kJ	2110	100	283
蛋白质Protein	g	11.9	0.56	1.6
乳清蛋白Whey	g	7.6	0.36	1.0
酪蛋白Casein	g	4.3	0.20	0.58
脂肪Fat	g	27.5	1.3	3.7
乳铁蛋白Lactoferrin	mg	40.0	1.9	5.4
维生素Vitamins				
维生素A Vitamin A	μgRE	558	26.4	74.7
维生素D Vitamin D	μg	7.6	0.36	1.0
维生素E Vitamin E	mgα-TE	9.1	0.43	1.2
维生素K_1 Vitamin K_1	μg	47.0	2.2	6.3
维生素B_1 Vitamin B_1	μg	643	30.5	86.1
维生素B_2 Vitamin B_2	μg	1120	53.1	150
维生素B_6 Vitamin B_6	μg	440	20.9	58.9
维生素B_{12} Vitamin B_{12}	μg	2.2	0.10	0.29
烟酸Niacin	μg	4075	193	546
叶酸Folic Acid	μg	79.0	3.7	10.6
泛酸Pantothenic Acid	μg	3560	169	477
维生素C Vitamin C	mg	152	7.2	20.4
生物素Biotin	μg	26.8	1.3	3.6
胆碱Choline	mg	126	6.0	16.9
肌醇Inositol	mg	51.5	2.4	6.9
矿物质Minerals				
钠Sodium	mg	173	8.2	23.2
钾Potassium	mg	485	23.0	64.9
铜Copper	μg	443	21.0	59.3
镁Magnesium	mg	55.5	2.6	7.4
铁Iron	mg	5.2	0.25	0.70
锌Zinc	mg	4.6	0.22	0.62
锰Manganese	μg	100	4.7	13.4
钙Calcium	mg	415	19.7	55.6
磷Phosphorus	mg	276	13.1	37.0
碘Iodine	μg	76.0	3.6	10.2
氯Chloride	mg	375	17.8	50.2
硒Selenium	μg	20.5	0.97	2.7

原装进口

akara™

爱瑞嘉®

金装婴儿配方奶粉

Purimilcare®
爱瑞嘉纯净亲润®配方

For Babies
From 0-6 Months
适用于0~6个月婴儿

1

净含量：900克

1

爱瑞嘉纯净亲润®配方

爱瑞嘉纯净亲润®配方奶粉从牧场到罐装，全程严格把控和监督，专为宝宝各阶段成长设计。

- 爱瑞嘉金装婴儿配方奶粉
  爱瑞嘉金装婴儿配方奶粉专为 0-6 个月宝宝设计，供母乳喂养不足的宝宝食用。爱瑞嘉纯净亲润®配方为宝宝成长阶段所需而设计。
- 爱瑞嘉金装较大婴儿配方奶粉
  爱瑞嘉金装较大婴儿配方奶粉专为 6-12 个月宝宝设计。爱瑞嘉纯净亲润®配方为宝宝成长发育阶段所需而设计。
- 爱瑞嘉金装幼儿配方奶粉
  爱瑞嘉金装幼儿配方奶粉专为 1-3 岁幼儿设计。爱瑞嘉纯净亲润®配方辅以宝宝成长阶段所需营养素。

过敏源提示

本产品含有牛奶蛋白、鱼类、大豆的成分。

冲调指南

在调奶前必须洗手。

1. 用沸水煮消毒器具消毒奶瓶、奶嘴和用具。
2. 饮用水烧开放冰到喂哺温度（约37℃）。
3. 将温开水倒入清毒过的奶瓶，测量好水量。
4. 轻轻装满勺子，用小刀抹平，不要压紧奶粉，加入所需的勺数。
5. 每50毫升水加一平勺奶粉，盖上奶瓶盖，摇动溶解奶粉。
6. 喂哺前滴几滴在手腕上检查温度是否合适。

原产国：新西兰
生产日期（MFD）：日/月/年（见罐底）
保质期至（EXP）：日/月/年（见罐底）
生产批号（LOT）：见罐底
生产商注册编号（REG）：540
生产商：Synlait Milk Limited
生产商地址：1028 Hesleton Road, RD13, Rakaia, Canterbury, New Zealand
中国进口商：四川新希望营养制品有限公司
进口商地址：新津县工业园区希望路88号
爱瑞嘉亲子热线：400-881-6090
爱瑞嘉官网：www.akaranutrition.com

NEW ZEALAND MADE

9 421028 300926

PPR100175

803760

PACKAGING DYNAMICS (AUST) PTY LTD

Jamestrong

JAMESTRONG CONTACT: Daniel Prenter
ARTWORK CREATION DATE: 20/08/14
CLIENT: Synlait
DESCRIPTION: Akara Step 1 900g
JOB CODE: PD803760
PDA JOB NUMBER: JN17180
TEMPLATE: 127 x 162.5 NZ
DATE LAST AMENDED: 31/04/15
BY ARTWORKER: Darren
SUPERCEDES CODE: 803873
DECORATION PLANT: KMP

COLOUR:

BASE: PRIME
WHITE SHARP
GOLD
WHITE OPEN
MAGENTA
YELLOW
CYAN
PURPLE
BLUE
BLACK

ALTERATIONS:
03/09/14: Changed artwork from Coat to Print White adding 2 x Whites, Changed PMS 3135 to process.
09/09/14: Rework artwork image colours to match that of supplied cans.
Previous Print.
31.04.15 - placed in new artwork.

PLATES AFFECTED:
31.04.15 - All Plates

TECHNICAL APPROVAL

NAME:
DATE:
PROOF: OK ○
SEPARATIONS: OK ○
COMMENTS:

GENERAL CHECKS

- ○ 2mm CLEARANCE FROM VARNISH EDGE (BODY ART) CHECKED
- ○ MAX ART LIMIT CHECKED & APPROVED
- ○ BARCODE COLOR & ORIENTATION APPROVED BY MANUFACTURING
- ○ ALL FONT SIZES CHECKED & APPROVED BY DECORATION
- ○ IF REQUIRED - GOLD INK OR VARNISH SPECIFIED

TRI-STATE LIMIT
W: 395.41mm x H: 167.00 mm
BASE COAT & VARNISH LIMIT (B,C)
L: 391.00 mm (B) x H: 162.00mm (C)
BASE COLOUR LIMIT (A,D)
L: 393.00mm (A) x H: 160.00mm (D)
MAXIMUM ARTWORK LIMIT -STANDARD OVERCAP (A,F)
L: 393.00 (A) x H: 149.00mm (F)
BARCODE LIMIT
L: 199.00mm x H: 84.30mm
NO OVERCAP
L: 393.00 (A) x H: 154.00mm (E)

Background color must not bleed past the 'base colour limit'.
Graphic elements must be contained within the 'maximum artwork limit'.

DISCLAIMER:

Please note that this proof is made by superimposing dyed photographic images of each colour over one another to produce the finished proof.

Whilst we endeavour to ensure that this proof is accurate in terms of content, we cannot guarantee that the printed image will match the proof for colour & shading although every attempt will be made to achieve target as close as possible.

Please check this proof thoroughly before signing.

If CUSTOMER requires a Colour match additional to the Digital Proof, Jamestrong Packaging can arrange on request - Ink Colour Roll-outs for Special and/or PMS colours.

CUSTOMER APPROVAL SECTION

NAME & DATE:
SIGNATURE: PROOF: OK ○
INK roll-outs Special and/or PMS Colours: OK ○
INK ORDERING AND PRINT PRODUCTION CANNOT BE PLANNED UNTIL SIGNED DIGITAL PROOF (and if requested signed ink roll-outs) ARE RECEIVED AT JAMESTRONG PACKAGING.
COMMENTS:

YOUR APPROVAL OF THIS PROOF WILL ACTION THE DESTRUCTION OF THE SUPERSEDED DESIGN PRINTING PLATES. OK ○

PART 7:
APPENDIX 6: Curriculum vitae of GRAS Panel Members

The data and information presented within Appendix 6 is Confidential to each of the GRAS Panel Members. It contains personal information and is **not generally available**.

TABLE OF CONTENTS

Adopted 1969. Amendment 1999. Revisions 1997 and 2003. Editorial corrections 2011.

INTRODUCTION

People have the right to expect the food they eat to be safe and suitable for consumption. Foodborne illness and foodborne injury are at best unpleasant; at worst, they can be fatal. But there are also other consequences. Outbreaks of foodborne illness can damage trade and tourism, and lead to loss of earnings, unemployment and litigation. Food spoilage is wasteful, costly and can adversely affect trade and consumer confidence.

International food trade, and foreign travel, are increasing, bringing important social and economic benefits. But this also makes the spread of illness around the world easier. Eating habits too, have undergone major change in many countries over the last two decades and new food production, preparation and distribution techniques have developed to reflect this. Effective hygiene control, therefore, is vital to avoid the adverse human health and economic consequences of foodborne illness, foodborne injury, and food spoilage. Everyone, including farmers and growers, manufacturers and processors, food handlers and consumers, has a responsibility to assure that food is safe and suitable for consumption.

These General Principles lay a firm foundation for ensuring food hygiene and should be used in conjunction with each specific code of hygienic practice, where appropriate, and the guidelines on microbiological criteria. The document follows the food chain from primary production through to final consumption, highlighting the key hygiene controls at each stage. It recommends a HACCP-based approach wherever possible to enhance food safety as described in *Hazard Analysis and Critical Control Point (HACCP) System and Guidelines for its Application* (Annex).

The controls described in this General Principles document are internationally recognized as essential to ensure the safety and suitability of food for consumption. The General Principles are commended to Governments, industry (including individual primary producers, manufacturers, processors, food service operators and retailers) and consumers alike.

SECTION I - OBJECTIVES

1.1 THE CODEX GENERAL PRINCIPLES OF FOOD HYGIENE:

- identify the essential principles of food hygiene applicable throughout the food chain (including primary production through to the final consumer), to achieve the goal of ensuring that food is safe and suitable for human consumption;
- recommend a HACCP-based approach as a means to enhance food safety;
- indicate how to implement those principles; and
- provide a guidance for specific codes which may be needed for - sectors of the food chain; processes; or commodities; to amplify the hygiene requirements specific to those areas.

SECTION II - SCOPE, USE AND DEFINITION

2.1 SCOPE

2.1.1 The food chain

This document follows the food chain from primary production to the final consumer, setting out the necessary hygiene conditions for producing food which is safe and suitable for consumption. The document provides a base-line structure for other, more specific, codes applicable to particular sectors. Such specific codes and guidelines should be read in conjunction with this document and *Hazard Analysis and Critical Control Point (HACCP) System and Guidelines for its Application* (Annex).

2.1.2 Roles of Governments, industry, and consumers

Governments can consider the contents of this document and decide how best they should encourage the implementation of these general principles to:

- protect consumers adequately from illness or injury caused by food; policies need to consider the vulnerability of the population, or of different groups within the population;
- provide assurance that food is suitable for human consumption;
- maintain confidence in internationally traded food; and
- provide health education programmes which effectively communicate the principles of food hygiene to industry and consumers.

Industry should apply the hygienic practices set out in this document to:

- provide food which is safe and suitable for consumption;
- ensure that consumers have clear and easily-understood information, by way of labelling and other appropriate means, to enable them to protect their food from contamination and growth/survival of foodborne pathogens by storing, handling and preparing it correctly; and
- maintain confidence in internationally traded food.

Consumers should recognize their role by following relevant instructions and applying appropriate food hygiene measures.

2.2 USE

Each section in this document states both the objectives to be achieved and the rationale behind those objectives in terms of the safety and suitability of food.

Section III covers primary production and associated procedures. Although hygiene practices may differ considerably for the various food commodities and specific codes should be applied where appropriate, some general guidance is given in this section. Sections IV to X set down the general hygiene principles which apply throughout the food chain to the point of sale. Section IX also covers consumer information, recognizing the important role played by consumers in maintaining the safety and suitability of food.

There will inevitably be situations where some of the specific requirements contained in this document are not applicable. The fundamental question in every case is "what is necessary and appropriate on the grounds of the safety and suitability of food for consumption?"

The text indicates where such questions are likely to arise by using the phrases "where necessary" and "where appropriate". In practice, this means that, although the requirement is generally appropriate and reasonable, there will nevertheless be some situations where it is neither necessary nor appropriate on the grounds of food safety and suitability. In deciding whether a requirement is necessary or appropriate, an assessment of the risk should be made, preferably within the framework of the HACCP approach. This approach allows the requirements in this document to be flexibly and sensibly applied with a proper regard for the overall objectives of producing food which is safe and suitable for consumption. In so doing it takes into account the wide diversity of activities and varying degrees of risk involved in producing food. Additional guidance is available in specific food codes.

2.3 DEFINITIONS

For the purpose of this Code, the following expressions have the meaning stated:

Cleaning - the removal of soil, food residue, dirt, grease or other objectionable matter.

Contaminant - any biological or chemical agent, foreign matter, or other substances not intentionally added to food which may compromise food safety or suitability.

Contamination - the introduction or occurrence of a contaminant in food or food environment.

Disinfection - the reduction, by means of chemical agents and/or physical methods, of the number of micro-organisms in the environment, to a level that does not compromise food safety or suitability.

Establishment - any building or area in which food is handled and the surroundings under the control of the same management.

Food hygiene - all conditions and measures necessary to ensure the safety and suitability of food at all stages of the food chain.

Hazard - a biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect.

HACCP - a system which identifies, evaluates, and controls hazards which are significant for food safety.

Food handler - any person who directly handles packaged or unpackaged food, food equipment and utensils, or food contact surfaces and is therefore expected to comply with food hygiene requirements

Food safety - assurance that food will not cause harm to the consumer when it is prepared and/or eaten according to its intended use.

Food suitability - assurance that food is acceptable for human consumption according to its intended use.

Primary production - those steps in the food chain up to and including, for example, harvesting, slaughter, milking, fishing.

SECTION III - PRIMARY PRODUCTION

OBJECTIVES:

Primary production should be managed in a way that ensures that food is safe and suitable for its intended use. Where necessary, this will include:

- avoiding the use of areas where the environment poses a threat to the safety of food;
- controlling contaminants, pests and diseases of animals and plants in such a way as not to pose a threat to food safety;
- adopting practices and measures to ensure food is produced under appropriately hygienic conditions.

RATIONALE:

To reduce the likelihood of introducing a hazard which may adversely affect the safety of food, or its suitability for consumption, at later stages of the food chain.

3.1 ENVIRONMENTAL HYGIENE

Potential sources of contamination from the environment should be considered. In particular, primary food production should not be carried on in areas where the presence of potentially harmful substances would lead to an unacceptable level of such substances in food.

3.2 HYGIENIC PRODUCTION OF FOOD SOURCES

The potential effects of primary production activities on the safety and suitability of food should be considered at all times. In particular, this includes identifying any specific points in such activities where a high probability of contamination may exist and taking specific measures to minimize that probability. The HACCP-based approach may assist in the taking of such measures - see *Hazard Analysis and Critical Control (HACCP) Point System and Guidelines for its Application* (Annex).

Producers should as far as practicable implement measures to:

- control contamination from air, soil, water, feedstuffs, fertilizers (including natural fertilizers), pesticides, veterinary drugs or any other agent used in primary production;
- control plant and animal health so that it does not pose a threat to human health through food consumption, or adversely affect the suitability of the product; and
- protect food sources from faecal and other contamination.

In particular, care should be taken to manage wastes, and store harmful substances appropriately. On-farm programmes which achieve specific food safety goals are becoming an important part of primary production and should be encouraged.

3.3 HANDLING, STORAGE AND TRANSPORT

Procedures should be in place to:

- sort food and food ingredients to segregate material which is evidently unfit for human consumption;
- dispose of any rejected material in a hygienic manner; and
- Protect food and food ingredients from contamination by pests, or by chemical, physical or microbiological contaminants or other objectionable substances during handling, storage and transport.

Care should be taken to prevent, so far as reasonably practicable, deterioration and spoilage through appropriate measures which may include controlling temperature, humidity, and/or other controls.

3.4 CLEANING, MAINTENANCE AND PERSONNEL HYGIENE AT PRIMARY PRODUCTION

Appropriate facilities and procedures should be in place to ensure that:

- any necessary cleaning and maintenance is carried out effectively; and
- an appropriate degree of personal hygiene is maintained.

SECTION IV - ESTABLISHMENT: DESIGN AND FACILITIES

OBJECTIVES:

Depending on the nature of the operations, and the risks associated with them, premises, equipment and facilities should be located, designed and constructed to ensure that:

- contamination is minimized;
- design and layout permit appropriate maintenance, cleaning and disinfections and minimize air-borne contamination;
- surfaces and materials, in particular those in contact with food, are non-toxic in intended use and, where necessary, suitably durable, and easy to maintain and clean;
- where appropriate, suitable facilities are available for temperature, humidity and other controls; and
- there is effective protection against pest access and harbourage.

RATIONALE:

Attention to good hygienic design and construction, appropriate location, and the provision of adequate facilities, is necessary to enable hazards to be effectively controlled.

4.1 LOCATION

4.1.1 Establishments

Potential sources of contamination need to be considered when deciding where to locate food establishments, as well as the effectiveness of any reasonable measures that might be taken to protect food. Establishments should not be located anywhere where, after considering such protective measures, it is clear that there will remain a threat to food safety or suitability. In particular, establishments should normally be located away from:

- environmentally polluted areas and industrial activities which pose a serious threat of contaminating food;

- areas subject to flooding unless sufficient safeguards are provided;
- areas prone to infestations of pests;
- areas where wastes, either solid or liquid, cannot be removed effectively.

4.1.2 Equipment

Equipment should be located so that it:

- permits adequate maintenance and cleaning;
- functions in accordance with its intended use; and
- facilitates good hygiene practices, including monitoring.

4.2 PREMISES AND ROOMS

4.2.1 Design and layout

Where appropriate, the internal design and layout of food establishments should permit good food hygiene practices, including protection against cross-contamination between and during operations by foodstuffs.

4.2.2 Internal structures and fittings

Structures within food establishments should be soundly built of durable materials and be easy to maintain, clean and where appropriate, able to be disinfected. In particular the following specific conditions should be satisfied where necessary to protect the safety and suitability of food:

- the surfaces of walls, partitions and floors should be made of impervious materials with no toxic effect in intended use;
- walls and partitions should have a smooth surface up to a height appropriate to the operation;
- floors should be constructed to allow adequate drainage and cleaning;
- ceilings and overhead fixtures should be constructed and finished to minimize the build up of dirt and condensation, and the shedding of particles;
- windows should be easy to clean, be constructed to minimize the build up of dirt and where necessary, be fitted with removable and cleanable insect-proof screens. Where necessary, windows should be fixed;
- doors should have smooth, non-absorbent surfaces, and be easy to clean and, where necessary, disinfect;
- working surfaces that come into direct contact with food should be in sound condition, durable and easy to clean, maintain and disinfect. They should be made of smooth, non-absorbent materials, and inert to the food, to detergents and disinfectants under normal operating conditions.

4.2.3 Temporary/mobile premises and vending machines

Premises and structures covered here include market stalls, mobile sales and street vending vehicles, temporary premises in which food is handled such as tents and marquees.

Such premises and structures should be sited, designed and constructed to avoid, as far as reasonably practicable, contaminating food and harbouring pests.

In applying these specific conditions and requirements, any food hygiene hazards associated with such facilities should be adequately controlled to ensure the safety and suitability of food.

4.3 EQUIPMENT

4.3.1 General

Equipment and containers (other than once-only use containers and packaging) coming into contact with food, should be designed and constructed to ensure that, where necessary, they can be adequately cleaned, disinfected and maintained to avoid the contamination of food. Equipment and containers should be made of materials with no toxic effect in intended use. Where necessary, equipment should be durable and movable or capable of being disassembled to allow for maintenance, cleaning, disinfection, monitoring and, for example, to facilitate inspection for pests.

4.3.2 Food control and monitoring equipment

In addition to the general requirements in paragraph 4.3.1, equipment used to cook, heat treat, cool, store or freeze food should be designed to achieve the required food temperatures as rapidly as necessary in the interests of food safety and suitability, and maintain them effectively. Such equipment should also be designed to allow temperatures to be monitored and controlled. Where necessary, such equipment should have effective means of controlling and monitoring humidity, air-flow and any other characteristic likely to have a detrimental effect on the safety or suitability of food. These requirements are intended to ensure that:

- harmful or undesirable micro-organisms or their toxins are eliminated or reduced to safe levels or their survival and growth are effectively controlled;
- where appropriate, critical limits established in HACCP-based plans can be monitored; and
- temperatures and other conditions necessary to food safety and suitability can be rapidly achieved and maintained.

4.3.3 Containers for waste and inedible substances

Containers for waste, by-products and inedible or dangerous substances, should be specifically identifiable, suitably constructed and, where appropriate, made of impervious material. Containers used to hold dangerous substances should be identified and, where appropriate, be lockable to prevent malicious or accidental contamination of food.

4.4 FACILITIES

4.4.1 Water supply

An adequate supply of potable water with appropriate facilities for its storage, distribution and temperature control, should be available whenever necessary to ensure the safety and suitability of food.

Potable water should be as specified in the latest edition of WHO Guidelines for Drinking Water Quality, or water of a higher standard. Non-potable water (for use in, for example, fire control, steam production, refrigeration and other similar purposes where it would not contaminate food), shall have a separate system. Non-potable water systems shall be identified and shall not connect with, or allow reflux into, potable water systems.

4.4.2 Drainage and waste disposal

Adequate drainage and waste disposal systems and facilities should be provided. They should be designed and constructed so that the risk of contaminating food or the potable water supply is avoided.

4.4.3 Cleaning

Adequate facilities, suitably designated, should be provided for cleaning food, utensils and equipment. Such facilities should have an adequate supply of hot and cold potable water where appropriate.

4.4.4 Personnel hygiene facilities and toilets

Personnel hygiene facilities should be available to ensure that an appropriate degree of personal hygiene can be maintained and to avoid contaminating food. Where appropriate, facilities should include:

- adequate means of hygienically washing and drying hands, including wash basins and a supply of hot and cold (or suitably temperature controlled) water;
- lavatories of appropriate hygienic design; and
- adequate changing facilities for personnel.

Such facilities should be suitably located and designated.

4.4.5 Temperature control

Depending on the nature of the food operations undertaken, adequate facilities should be available for heating, cooling, cooking, refrigerating and freezing food, for storing refrigerated or frozen foods, monitoring food temperatures, and when necessary, controlling ambient temperatures to ensure the safety and suitability of food.

4.4.6 Air quality and ventilation

Adequate means of natural or mechanical ventilation should be provided, in particular to:

- minimize air-borne contamination of food, for example, from aerosols and condensation droplets;
- control ambient temperatures;
- control odours which might affect the suitability of food; and
- control humidity, where necessary, to ensure the safety and suitability of food.

Ventilation systems should be designed and constructed so that air does not flow from contaminated areas to clean areas and, where necessary, they can be adequately maintained and cleaned.

4.4.7 Lighting

Adequate natural or artificial lighting should be provided to enable the undertaking to operate in a hygienic manner. Where necessary, lighting should not be such that the resulting colour is misleading. The intensity should be adequate to the nature of the operation. Lighting fixtures should, where appropriate, be protected to ensure that food is not contaminated by breakages.

4.4.8 Storage

Where necessary, adequate facilities for the storage of food, ingredients and non-food chemicals (e.g. cleaning materials, lubricants, fuels) should be provided.

Where appropriate, food storage facilities should be designed and constructed to:

- permit adequate maintenance and cleaning;
- avoid pest access and harbourage;
- enable food to be effectively protected from contamination during storage; and
- where necessary, provide an environment which minimizes the deterioration of food (e.g. by temperature and humidity control).

The type of storage facilities required will depend on the nature of the food. Where necessary, separate, secure storage facilities for cleaning materials and hazardous substances should be provided.

SECTION V - CONTROL OF OPERATION

OBJECTIVE:

To produce food which is safe and suitable for human consumption by:

- formulating design requirements with respect to raw materials, composition, processing, distribution, and consumer use to be met in the manufacture and handling of specific food items; and
- designing, implementing, monitoring and reviewing effective control systems.

RATIONALE:

To reduce the risk of unsafe food by taking preventive measures to assure the safety and suitability of food at an appropriate stage in the operation by controlling food hazards.

5.1 CONTROL OF FOOD HAZARDS

Food business operators should control food hazards through the use of systems such as HACCP. They should:

- **identify** any steps in their operations which are critical to the safety of food;
- **implement** effective control procedures at those steps;
- **monitor** control procedures to ensure their continuing effectiveness; and
- **review** control procedures periodically, and whenever the operations change.

These systems should be applied throughout the food chain to control food hygiene throughout the shelf-life of the product through proper product and process design.

Control procedures may be simple, such as checking stock rotation calibrating equipment, or correctly loading refrigerated display units. In some cases a system based on expert advice, and involving documentation, may be appropriate. A model of such a food safety system is described in *Hazard Analysis and Critical Control (HACCP) System and Guidelines for its Application* (Annex).

5.2 KEY ASPECTS OF HYGIENE CONTROL SYSTEMS

5.2.1 Time and temperature control

Inadequate food temperature control is one of the most common causes of foodborne illness or food spoilage. Such controls include time and temperature of cooking, cooling, processing and storage. Systems should be in place to ensure that temperature is controlled effectively where it is critical to the safety and suitability of food.

Temperature control systems should take into account:

- the nature of the food, e.g. its water activity, pH, and likely initial level and types of micro-organisms;
- the intended shelf-life of the product;
- the method of packaging and processing; and
- how the product is intended to be used, e.g. further cooking/processing or ready-to-eat.

Such systems should also specify tolerable limits for time and temperature variations.

Temperature recording devices should be checked at regular intervals and tested for accuracy.

5.2.2 Specific process steps

Other steps which contribute to food hygiene may include, for example:

- chilling
- thermal processing
- irradiation
- drying
- chemical preservation
- vacuum or modified atmospheric packaging

5.2.3 Microbiological and other specifications

Management systems described in paragraph 5.1 offer an effective way of ensuring the safety and suitability of food. Where microbiological, chemical or physical specifications are used in any food control system, such specifications should be based on sound scientific principles and state, where appropriate, monitoring procedures, analytical methods and action limits.

5.2.4 Microbiological cross-contamination

Pathogens can be transferred from one food to another, either by direct contact or by food handlers, contact surfaces or the air. Raw, unprocessed food should be effectively separated, either physically or by time, from ready-to-eat foods, with effective intermediate cleaning and where appropriate disinfection.

Access to processing areas may need to be restricted or controlled. Where risks are particularly high, access to processing areas should be only via a changing facility. Personnel may need to be required to put on clean protective clothing including footwear and wash their hands before entering.

Surfaces, utensils, equipment, fixtures and fittings should be thoroughly cleaned and where necessary disinfected after raw food, particularly meat and poultry, has been handled or processed.

5.2.5 Physical and chemical contamination

Systems should be in place to prevent contamination of foods by foreign bodies such as glass or metal shards from machinery, dust, harmful fumes and unwanted chemicals. In manufacturing and processing, suitable detection or screening devices should be used where necessary.

5.3 INCOMING MATERIAL REQUIREMENTS

No raw material or ingredient should be accepted by an establishment if it is known to contain parasites, undesirable micro-organisms, pesticides, veterinary drugs or toxic, decomposed or extraneous substances which would not be reduced to an acceptable level by normal sorting and/or processing. Where appropriate, specifications for raw materials should be identified and applied.

Raw materials or ingredients should, where appropriate, be inspected and sorted before processing. Where necessary, laboratory tests should be made to establish fitness for use. Only sound, suitable raw materials or ingredients should be used.

Stocks of raw materials and ingredients should be subject to effective stock rotation.

5.4 PACKAGING

Packaging design and materials should provide adequate protection for products to minimize contamination, prevent damage, and accommodate proper labelling. Packaging materials or gases where used must be non-toxic and not pose a threat to the safety and suitability of food under the specified conditions of storage and use. Where appropriate, reusable packaging should be suitably durable, easy to clean and, where necessary, disinfect.

5.5 WATER

5.5.1 In contact with food

Only potable water, should be used in food handling and processing, with the following exceptions:

- for steam production, fire control and other similar purposes not connected with food; and
- in certain food processes, e.g. chilling, and in food handling areas, provided this does not constitute a hazard to the safety and suitability of food (e.g. the use of clean sea water).

Water recirculated for reuse should be treated and maintained in such a condition that no risk to the safety and suitability of food results from its use. The treatment process should be effectively monitored. Recirculated water which has received no further treatment and water recovered from processing of food by evaporation or drying may be used, provided its use does not constitute a risk to the safety and suitability of food.

5.5.2 As an ingredient

Potable water should be used wherever necessary to avoid food contamination.

5.5.3 Ice and steam

Ice should be made from water that complies with section 4.4.1. Ice and steam should be produced, handled and stored to protect them from contamination.

Steam used in direct contact with food or food contact surfaces should not constitute a threat to the safety and suitability of food.

5.6 MANAGEMENT AND SUPERVISION

The type of control and supervision needed will depend on the size of the business, the nature of its activities and the types of food involved. Managers and supervisors should have enough knowledge of food hygiene principles and practices to be able to judge potential risks, take appropriate preventive and corrective action, and ensure that effective monitoring and supervision takes place.

5.7 DOCUMENTATION AND RECORDS

Where necessary, appropriate records of processing, production and distribution should be kept and retained for a period that exceeds the shelf-life of the product. Documentation can enhance the credibility and effectiveness of the food safety control system.

5.8 RECALL PROCEDURES

Managers should ensure effective procedures are in place to deal with any food safety hazard and to enable the complete, rapid recall of any implicated lot of the finished food from the market. Where a product has been withdrawn

because of an immediate health hazard, other products which are produced under similar conditions, and which may present a similar hazard to public health, should be evaluated for safety and may need to be withdrawn. The need for public warnings should be considered.

Recalled products should be held under supervision until they are destroyed, used for purposes other than human consumption, determined to be safe for human consumption, or reprocessed in a manner to ensure their safety.

SECTION VI - ESTABLISHMENT: MAINTENANCE AND SANITATION

OBJECTIVE:

To establish effective systems to:

- ensure adequate and appropriate maintenance and cleaning;
- control pests;
- manage waste; and
- monitor effectiveness of maintenance and sanitation procedures.

RATIONALE:

To facilitate the continuing effective control of food hazards, pests, and other agents likely to contaminate food.

6.1 MAINTENANCE AND CLEANING

6.1.1 General

Establishments and equipment should be kept in an appropriate state of repair and condition to:

- facilitate all sanitation procedures;
- function as intended, particularly at critical steps (see paragraph 5.1);
- prevent contamination of food, e.g. from metal shards, flaking plaster, debris and chemicals.

Cleaning should remove food residues and dirt which may be a source of contamination. The necessary cleaning methods and materials will depend on the nature of the food business. Disinfection may be necessary after cleaning.

Cleaning chemicals should be handled and used carefully and in accordance with manufacturers' instructions and stored, where necessary, separated from food, in clearly identified containers to avoid the risk of contaminating food.

6.1.2 Cleaning procedures and methods

Cleaning can be carried out by the separate or the combined use of physical methods, such as heat, scrubbing, turbulent flow, vacuum cleaning or other methods that avoid the use of water, and chemical methods using detergents, alkalis or acids.

Cleaning procedures will involve, where appropriate:

- removing gross debris from surfaces;
- applying a detergent solution to loosen soil and bacterial film and hold them in solution or suspension;
- rinsing with water which complies with section 4, to remove loosened soil and residues of detergent;
- dry cleaning or other appropriate methods for removing and collecting residues and debris; and
- where necessary, disinfection with subsequent rinsing unless the manufacturers' instructions indicate on scientific basis that rinsing is not required.

6.2 CLEANING PROGRAMMES

Cleaning and disinfection programmes should ensure that all parts of the establishment are appropriately clean, and should include the cleaning of cleaning equipment.

Cleaning and disinfection programmes should be continually and effectively monitored for their suitability and effectiveness and where necessary, documented.

Where written cleaning programmes are used, they should specify:

- areas, items of equipment and utensils to be cleaned;
- responsibility for particular tasks;
- method and frequency of cleaning; and
- monitoring arrangements.

Where appropriate, programmes should be drawn up in consultation with relevant specialist expert advisors.

6.3 PEST CONTROL SYSTEMS

6.3.1 General

Pests pose a major threat to the safety and suitability of food. Pest infestations can occur where there are breeding sites and a supply of food. Good hygiene practices should be employed to avoid creating an environment conducive to pests. Good sanitation, inspection of incoming materials and good monitoring can minimize the likelihood of infestation and thereby limit the need for pesticides.

6.3.2 Preventing access

Buildings should be kept in good repair and condition to prevent pest access and to eliminate potential breeding sites. Holes, drains and other places where pests are likely to gain access should be kept sealed. Wire mesh screens, for example on open windows, doors and ventilators, will reduce the problem of pest entry. Animals should, wherever possible, be excluded from the grounds of factories and food processing plants.

6.3.3 Harbourage and infestation

The availability of food and water encourages pest harbourage and infestation. Potential food sources should be stored in pest-proof containers and/or stacked above the ground and away from walls. Areas both inside and outside food premises should be kept clean. Where appropriate, refuse should be stored in covered, pest-proof containers.

6.3.4 Monitoring and detection

Establishments and surrounding areas should be regularly examined for evidence of infestation.

6.3.5 Eradication

Pest infestations should be dealt with immediately and without adversely affecting food safety or suitability. Treatment with chemical, physical or biological agents should be carried out without posing a threat to the safety or suitability of food.

6.4 WASTE MANAGEMENT

Suitable provision must be made for the removal and storage of waste. Waste must not be allowed to accumulate in food handling, food storage, and other working areas and the adjoining environment except so far as is unavoidable for the proper functioning of the business.

Waste stores must be kept appropriately clean.

6.5 MONITORING EFFECTIVENESS

Sanitation systems should be monitored for effectiveness, periodically verified by means such as audit pre-operational inspections or, where appropriate, microbiological sampling of environment and food contact surfaces and regularly reviewed and adapted to reflect changed circumstances.

SECTION VII - ESTABLISHMENT: PERSONAL HYGIENE

OBJECTIVES:

To ensure that those who come directly or indirectly into contact with food are not likely to contaminate food by:

- maintaining an appropriate degree of personal cleanliness;
- behaving and operating in an appropriate manner.

RATIONALE:

People who do not maintain an appropriate degree of personal cleanliness, who have certain illnesses or conditions or who behave inappropriately, can contaminate food and transmit illness to consumers.

7.1 HEALTH STATUS

People known, or suspected, to be suffering from, or to be a carrier of a disease or illness likely to be transmitted through food, should not be allowed to enter any food handling area if there is a likelihood of their contaminating food. Any person so affected should immediately report illness or symptoms of illness to the management.

Medical examination of a food handler should be carried out if clinically or epidemiologically indicated.

7.2 ILLNESS AND INJURIES

Conditions which should be reported to management so that any need for medical examination and/or possible exclusion from food handling can be considered, include:

- jaundice;
- diarrhoea;
- vomiting;
- fever;
- sore throat with fever;

- visibly infected skin lesions (boils, cuts, etc.);
- discharges from the ear, eye or nose.

7.3 PERSONAL CLEANLINESS

Food handlers should maintain a high degree of personal cleanliness and, where appropriate, wear suitable protective clothing, head covering, and footwear. Cuts and wounds, where personnel are permitted to continue working, should be covered by suitable waterproof dressings.

Personnel should always wash their hands when personal cleanliness may affect food safety, for example:

- at the start of food handling activities;
- immediately after using the toilet; and
- after handling raw food or any contaminated material, where this could result in contamination of other food items; they should avoid handling ready-to-eat food, where appropriate.

7.4 PERSONAL BEHAVIOUR

People engaged in food handling activities should refrain from behaviour which could result in contamination of food, for example:

- smoking;
- spitting;
- chewing or eating;
- sneezing or coughing over unprotected food.

Personal effects such as jewellery, watches, pins or other items should not be worn or brought into food handling areas if they pose a threat to the safety and suitability of food.

7.5 VISITORS

Visitors to food manufacturing, processing or handling areas should, where appropriate, wear protective clothing and adhere to the other personal hygiene provisions in this section.

SECTION VIII - TRANSPORTATION

OBJECTIVES:

Measures should be taken where necessary to:

- protect food from potential sources of contamination;
- protect food from damage likely to render the food unsuitable for consumption; and
- provide an environment which effectively controls the growth of pathogenic or spoilage micro-organisms and the production of toxins in food.

RATIONALE:

Food may become contaminated, or may not reach its destination in a suitable condition for consumption, unless effective control measures are taken during transport, even where adequate hygiene control measures have been taken earlier in the food chain.

8.1 GENERAL

Food must be adequately protected during transport. The type of conveyances or containers required depends on the nature of the food and the conditions under which it has to be transported.

8.2 REQUIREMENTS

Where necessary, conveyances and bulk containers should be designed and constructed so that they:

- do not contaminate foods or packaging;
- can be effectively cleaned and, where necessary, disinfected;
- permit effective separation of different foods or foods from non-food items where necessary during transport;
- provide effective protection from contamination, including dust and fumes;
- can effectively maintain the temperature, humidity, atmosphere and other conditions necessary to protect food from harmful or undesirable microbial growth and deterioration likely to render it unsuitable for consumption; and
- allow any necessary temperature, humidity and other conditions to be checked.

8.3 USE AND MAINTENANCE

Conveyances and containers for transporting food should be kept in an appropriate state of cleanliness, repair and condition. Where the same conveyance or container is used for transporting different foods, or non-foods, effective cleaning and, where necessary, disinfection should take place between loads.

Where appropriate, particularly in bulk transport, containers and conveyances should be designated and marked for food use only and be used only for that purpose.

SECTION IX - PRODUCT INFORMATION AND CONSUMER AWARENESS

OBJECTIVES:

Products should bear appropriate information to ensure that:

- adequate and accessible information is available to the next person in the food chain to enable them to handle, store, process, prepare and display the product safely and correctly;
- the lot or batch can be easily identified and recalled if necessary.

Consumers should have enough knowledge of food hygiene to enable them to:

- understand the importance of product information;
- make informed choices appropriate to the individual; and
- prevent contamination and growth or survival of foodborne pathogens by storing, preparing and using it correctly.

Information for industry or trade users should be clearly distinguishable from consumer information, particularly on food labels.

RATIONALE:

Insufficient product information, and/or inadequate knowledge of general food hygiene, can lead to products being mishandled at later stages in the food chain. Such mishandling can result in illness, or products becoming unsuitable for consumption, even where adequate hygiene control measures have been taken earlier in the food chain.

9.1 LOT IDENTIFICATION

Lot identification is essential in product recall and also helps effective stock rotation. Each container of food should be permanently marked to identify the producer and the lot. Codex General Standard for the Labelling of Prepackaged Foods (CODEX STAN 1-1985, Rev. 1(1991)) applies.

9.2 PRODUCT INFORMATION

All food products should be accompanied by or bear adequate information to enable the next person in the food chain to handle, display, store and prepare and use the product safely and correctly.

9.3 LABELLING

Prepackaged foods should be labelled with clear instructions to enable the next person in the food chain to handle, display, store and use the product safely. Codex General Standard for the Labelling of Prepackaged Foods (CODEX STAN 1-1985, Rev. (1991)) applies.

9.4 CONSUMER EDUCATION

Health education programmes should cover general food hygiene. Such programmes should enable consumers to understand the importance of any product information and to follow any instructions accompanying products, and make informed choices. In particular consumers should be informed of the relationship between time/temperature control and foodborne illness.

SECTION X - TRAINING

OBJECTIVE:

Those engaged in food operations who come directly or indirectly into contact with food should be trained, and/or instructed in food hygiene to a level appropriate to the operations they are to perform.

RATIONALE:

Training is fundamentally important to any food hygiene system.

Inadequate hygiene training, and/or instruction and supervision of *all* people involved in food related activities pose a potential threat to the safety of food and its suitability for consumption.

10.1 AWARENESS AND RESPONSIBILITIES

Food hygiene training is fundamentally important. All personnel should be aware of their role and responsibility in protecting food from contamination or deterioration. Food handlers should have the necessary knowledge and skills to enable them to handle food hygienically. Those who handle strong cleaning chemicals or other potentially hazardous chemicals should be instructed in safe handling techniques.

10.2 TRAINING PROGRAMMES

Factors to take into account in assessing the level of training required include:

- the nature of the food, in particular its ability to sustain growth of pathogenic or spoilage micro-organisms;
- the manner in which the food is handled and packed, including the probability of contamination;
- the extent and nature of processing or further preparation before final consumption;
- the conditions under which the food will be stored; and
- the expected length of time before consumption.

10.3 INSTRUCTION AND SUPERVISION

Periodic assessments of the effectiveness of training and instruction programmes should be made, as well as routine supervision and checks to ensure that procedures are being carried out effectively.

Managers and supervisors of food processes should have the necessary knowledge of food hygiene principles and practices to be able to judge potential risks and take the necessary action to remedy deficiencies.

10.4 REFRESHER TRAINING

Training programmes should be routinely reviewed and updated where necessary. Systems should be in place to ensure that food handlers remain aware of all procedures necessary to maintain the safety and suitability of food.

HAZARD ANALYSIS AND CRITICAL CONTROL POINT (HACCP) SYSTEM AND GUIDELINES FOR ITS APPLICATION

ANNEX TO CAC/RCP 1-1969 (REV. 4 - 2003)

PREAMBLE

The first section of this document sets out the principles of the Hazard Analysis and Critical Control Point (HACCP) system adopted by the Codex Alimentarius Commission. The second section provides general guidance for the application of the system while recognizing that the details of application may vary depending on the circumstances of the food operation.[1]

The HACCP system, which is science based and systematic, identifies specific hazards and measures for their control to ensure the safety of food. HACCP is a tool to assess hazards and establish control systems that focus on prevention rather than relying mainly on end-product testing. Any HACCP system is capable of accommodating change, such as advances in equipment design, processing procedures or technological developments.

HACCP can be applied throughout the food chain from primary production to final consumption and its implementation should be guided by scientific evidence of risks to human health. As well as enhancing food safety, implementation of HACCP can provide other significant benefits. In addition, the application of HACCP systems can aid inspection by regulatory authorities and promote international trade by increasing confidence in food safety.

The successful application of HACCP requires the full commitment and involvement of management and the work force. It also requires a multidisciplinary approach; this multidisciplinary approach should include, when appropriate, expertise in agronomy, veterinary health, production, microbiology, medicine, public health, food technology, environmental health, chemistry and engineering, according to the particular study. The application of HACCP is compatible with the implementation of quality management systems, such as the ISO 9000 series, and is the system of choice in the management of food safety within such systems.

While the application of HACCP to food safety was considered here, the concept can be applied to other aspects of food quality.

DEFINITIONS

Control (verb): To take all necessary actions to ensure and maintain compliance with criteria established in the HACCP plan.

Control (noun): The state wherein correct procedures are being followed and criteria are being met.

Control measure: Any action and activity that can be used to prevent or eliminate a food safety hazard or reduce it to an acceptable level.

Corrective action: Any action to be taken when the results of monitoring at the CCP indicate a loss of control.

Critical Control Point (CCP): A step at which control can be applied and is essential to prevent or eliminate a food safety hazard or reduce it to an acceptable level.

Critical limit: A criterion which separates acceptability from unacceptability.

Deviation: Failure to meet a critical limit.

Flow diagram: A systematic representation of the sequence of steps or operations used in the production or manufacture of a particular food item.

HACCP: A system which identifies, evaluates, and controls hazards which are significant for food safety.

HACCP plan: A document prepared in accordance with the principles of HACCP to ensure control of hazards which are significant for food safety in the segment of the food chain under consideration.

Hazard: A biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect.

Hazard analysis: The process of collecting and evaluating information on hazards and conditions leading to their presence to decide which are significant for food safety and therefore should be addressed in the HACCP plan.

Monitor: The act of conducting a planned sequence of observations or measurements of control parameters to assess whether a CCP is under control.

Step: A point, procedure, operation or stage in the food chain including raw materials, from primary production to final consumption.

Validation: Obtaining evidence that the elements of the HACCP plan are effective.

Verification: The application of methods, procedures, tests and other evaluations, in addition to monitoring to determine compliance with the HACCP plan.

PRINCIPLES OF THE HACCP SYSTEM

The HACCP system consists of the following seven principles:

---

[1] The Principles of the HACCP System set the basis for the requirements for the application of HACCP, while the Guidelines for the Application provide general guidance for practical application.

PRINCIPLE 1

Conduct a hazard analysis.

PRINCIPLE 2

Determine the Critical Control Points (CCPs).

PRINCIPLE 3

Establish critical limit(s).

PRINCIPLE 4

Establish a system to monitor control of the CCP.

PRINCIPLE 5

Establish the corrective action to be taken when monitoring indicates that a particular CCP is not under control.

PRINCIPLE 6

Establish procedures for verification to confirm that the HACCP system is working effectively.

PRINCIPLE 7

Establish documentation concerning all procedures and records appropriate to these principles and their application.

GUIDELINES FOR THE APPLICATION OF THE HACCP SYSTEM

INTRODUCTION

Prior to application of HACCP to any sector of the food chain, that sector should have in place prerequisite programs such as good hygienic practices according to the Codex General Principles of Food Hygiene, the appropriate Codex Codes of Practice, and appropriate food safety requirements. These prerequisite programs to HACCP, including training, should be well established, fully operational and verified in order to facilitate the successful application and implementation of the HACCP system.

For all types of food business, management awareness and commitment is necessary for implementation of an effective HACCP system. The effectiveness will also rely upon management and employees having the appropriate HACCP knowledge and skills.

During hazard identification, evaluation, and subsequent operations in designing and applying HACCP systems, consideration must be given to the impact of raw materials, ingredients, food manufacturing practices, role of manufacturing processes to control hazards, likely end-use of the product, categories of consumers of concern, and epidemiological evidence relative to food safety.

The intent of the HACCP system is to focus control at Critical Control Points (CCPs). Redesign of the operation should be considered if a hazard which must be controlled is identified but no CCPs are found.

HACCP should be applied to each specific operation separately. CCPs identified in any given example in any Codex Code of Hygienic Practice might not be the only ones identified for a specific application or might be of a different nature. The HACCP application should be reviewed and necessary changes made when any modification is made in the product, process, or any step.

The application of the HACCP principles should be the responsibility of each individual businesses. However, it is recognised by governments and businesses that there may be obstacles that hinder the effective application of the HACCP principles by individual business. This is particularly relevant in small and/or less developed businesses. While it is recognized that when applying HACCP, flexibility appropriate to the business is important, all seven principles must be applied in the HACCP system. This flexibility should take into account the nature and size of the operation, including the human and financial resources, infrastructure, processes, knowledge and practical constraints.

Small and/or less developed businesses do not always have the resources and the necessary expertise on site for the development and implementation of an effective HACCP plan. In such situations, expert advice should be obtained from other sources, which may include: trade and industry associations, independent experts and regulatory authorities. HACCP literature and especially sector-specific HACCP guides can be valuable. HACCP guidance developed by experts relevant to the process or type of operation may provide a useful tool for businesses in designing and implementing the HACCP plan. Where businesses are using expertly developed HACCP guidance, it is essential that it is specific to the foods and/or processes under consideration. More detailed information on the obstacles in implementing HACCP, particularly in reference to SLDBs, and recommendations in resolving these obstacles, can be found in “Obstacles to the Application of HACCP, Particularly in Small and Less Developed Businesses, and Approaches to Overcome Them” (document in preparation by FAO/WHO).

The efficacy of any HACCP system will nevertheless rely on management and employees having the appropriate HACCP knowledge and skills, therefore ongoing training is necessary for all levels of employees and managers, as appropriate.

APPLICATION

The application of HACCP principles consists of the following tasks as identified in the Logic Sequence for Application of HACCP (Diagram 1).

1. ASSEMBLE HACCP TEAM

The food operation should assure that the appropriate product specific knowledge and expertise is available for the development of an effective HACCP plan. Optimally, this may be accomplished by assembling a multidisciplinary team. Where such expertise is not available on site, expert advice should be obtained from other sources, such as, trade and industry associations, independent experts, regulatory authorities, HACCP literature and HACCP guidance (including sector-specific HACCP guides). It may be possible that a well-trained individual with access to such guidance is able to implement HACCP in-house. The scope of the HACCP plan should be identified. The scope should describe which segment of the food chain is involved and the general classes of hazards to be addressed (e.g. does it cover all classes of hazards or only selected classes).

2. DESCRIBE PRODUCT

A full description of the product should be drawn up, including relevant safety information such as: composition, physical/chemical structure (including A_w, pH, etc), microcidal/static treatments (heat-treatment, freezing, brining, smoking, etc), packaging, durability and storage conditions and method of distribution. Within businesses with multiple products, for example, catering operations, it may be effective to group products with similar characteristics or processing steps, for the purpose of development of the HACCP plan.

3. IDENTIFY INTENDED USE

The intended use should be based on the expected uses of the product by the end user or consumer. In specific cases, vulnerable groups of the population, e.g. institutional feeding, may have to be considered.

4. CONSTRUCT FLOW DIAGRAM

The flow diagram should be constructed by the HACCP team (see also paragraph 1 above). The flow diagram should cover all steps in the operation for a specific product. The same flow diagram may be used for a number of products that are manufactured using similar processing steps. When applying HACCP to a given operation, consideration should be given to steps preceding and following the specified operation.

5. ON-SITE CONFIRMATION OF FLOW DIAGRAM

Steps must be taken to confirm the processing operation against the flow diagram during all stages and hours of operation and amend the flow diagram where appropriate. The confirmation of the flow diagram should be performed by a person or persons with sufficient knowledge of the processing operation.

6. LIST ALL POTENTIAL HAZARDS ASSOCIATED WITH EACH STEP, CONDUCT A HAZARD ANALYSIS, AND CONSIDER ANY MEASURES TO CONTROL IDENTIFIED HAZARDS

(SEE PRINCIPLE 1)

The HACCP team (see "assemble HACCP team" above) should list all of the hazards that may be reasonably expected to occur at each step according to the scope from primary production, processing, manufacture, and distribution until the point of consumption.

The HACCP team (see "assemble HACCP team") should next conduct a hazard analysis to identify for the HACCP plan, which hazards are of such a nature that their elimination or reduction to acceptable levels is essential to the production of a safe food.

In conducting the hazard analysis, wherever possible the following should be included:

- the likely occurrence of hazards and severity of their adverse health effects;
- the qualitative and/or quantitative evaluation of the presence of hazards;
- survival or multiplication of micro-organisms of concern;
- production or persistence in foods of toxins, chemicals or physical agents; and,
- conditions leading to the above.

Consideration should be given to what control measures, if any exist, can be applied to each hazard.

More than one control measure may be required to control a specific hazard(s) and more than one hazard may be controlled by a specified control measure.

7. DETERMINE CRITICAL CONTROL POINTS

(SEE PRINCIPLE 2)[2]

There may be more than one CCP at which control is applied to address the same hazard. The determination of a CCP in the HACCP system can be facilitated by the application of a decision tree (e.g., Diagram 2), which indicates a logic reasoning approach. Application of a decision tree should be flexible, given whether the operation is for production, slaughter, processing, storage, distribution or other. It should be used for guidance when determining CCPs. This example of a decision tree may not be applicable to all situations. Other approaches may be used. Training in the application of the decision tree is recommended.

If a hazard has been identified at a step where control is necessary for safety, and no control measure exists at that step, or any other, then the product or process should be modified at that step, or at any earlier or later stage, to include a control measure.

8. ESTABLISH CRITICAL LIMITS FOR EACH CCP

(SEE PRINCIPLE 3)

Critical limits must be specified and validated for each Critical Control Point. In some cases more than one critical limit will be elaborated at a particular step. Criteria often used include measurements of temperature, time, moisture level, pH, A_w, available chlorine, and sensory parameters such as visual appearance and texture.

Where HACCP guidance developed by experts has been used to establish the critical limits, care should be taken to ensure that these limits fully apply to the specific operation, product or groups of products under consideration. These critical limits should be measurable.

9. ESTABLISH A MONITORING SYSTEM FOR EACH CCP

(SEE PRINCIPLE 4)

Monitoring is the scheduled measurement or observation of a CCP relative to its critical limits. The monitoring procedures must be able to detect loss of control at the CCP. Further, monitoring should ideally provide this information in time to make adjustments to ensure control of the process to prevent violating the critical limits. Where possible, process adjustments should be made when monitoring results indicate a trend towards loss of control at a CCP. The adjustments should be taken before a deviation occurs. Data derived from monitoring must be evaluated by a designated person with knowledge and authority to carry out corrective actions when indicated. If monitoring is not

[2] Since the publication of the decision tree by Codex, its use has been implemented many times for training purposes. In many instances, while this tree has been useful to explain the logic and depth of understanding needed to determine CCPs, it is not specific to all food operations, e.g., slaughter, and therefore it should be used in conjunction with professional judgement, and modified in some cases.

continuous, then the amount or frequency of monitoring must be sufficient to guarantee the CCP is in control. Most monitoring procedures for CCPs will need to be done rapidly because they relate to on-line processes and there will not be time for lengthy analytical testing. Physical and chemical measurements are often preferred to microbiological testing because they may be done rapidly and can often indicate the microbiological control of the product.

All records and documents associated with monitoring CCPs must be signed by the person(s) doing the monitoring and by a responsible reviewing official(s) of the company.

10. ESTABLISH CORRECTIVE ACTIONS

(SEE PRINCIPLE 5)

Specific corrective actions must be developed for each CCP in the HACCP system in order to deal with deviations when they occur.

The actions must ensure that the CCP has been brought under control. Actions taken must also include proper disposition of the affected product. Deviation and product disposition procedures must be documented in the HACCP record keeping.

11. ESTABLISH VERIFICATION PROCEDURES

(SEE PRINCIPLE 6)

Establish procedures for verification. Verification and auditing methods, procedures and tests, including random sampling and analysis, can be used to determine if the HACCP system is working correctly. The frequency of verification should be sufficient to confirm that the HACCP system is working effectively.

Verification should be carried out by someone other than the person who is responsible for performing the monitoring and corrective actions. Where certain verification activities cannot be performed in house, verification should be performed on behalf of the business by external experts or qualified third parties.

Examples of verification activities include:

- Review of the HACCP system and plan and its records;
- Review of deviations and product dispositions;
- Confirmation that CCPs are kept under control.

Where possible, validation activities should include actions to confirm the efficacy of all elements of the HACCP system.

12. ESTABLISH DOCUMENTATION AND RECORD KEEPING

(SEE PRINCIPLE 7)

Efficient and accurate record keeping is essential to the application of a HACCP system. HACCP procedures should be documented. Documentation and record keeping should be appropriate to the nature and size of the operation and sufficient to assist the business to verify that the HACCP controls are in place and being maintained. Expertly developed HACCP guidance materials (e.g. sector-specific HACCP guides) may be utilised as part of the documentation, provided that those materials reflect the specific food operations of the business.

Documentation examples are:

Hazard analysis;

CCP determination;

Critical limit determination.

Record examples are:

- CCP monitoring activities;
- Deviations and associated corrective actions;
- Verification procedures performed;
- Modifications to the HACCP plan;

An example of a HACCP worksheet for the development of a HACCP plan is attached as Diagram 3.

A simple record-keeping system can be effective and easily communicated to employees. It may be integrated into existing operations and may use existing paperwork, such as delivery invoices and checklists to record, for example, product temperatures.

TRAINING

Training of personnel in industry, government and academia in HACCP principles and applications and increasing awareness of consumers are essential elements for the effective implementation of HACCP. As an aid in developing specific training to support a HACCP plan, working instructions and procedures should be developed which define the tasks of the operating personnel to be stationed at each Critical Control Point.

Cooperation between primary producer, industry, trade groups, consumer organisations, and responsible authorities is of vital important. Opportunities should be provided for the joint training of industry and control authorities to encourage and maintain a continuous dialogue and create a climate of understanding in the practical application of HACCP.

DIAGRAM 1

LOGIC SEQUENCE FOR APPLICATION OF HACCP

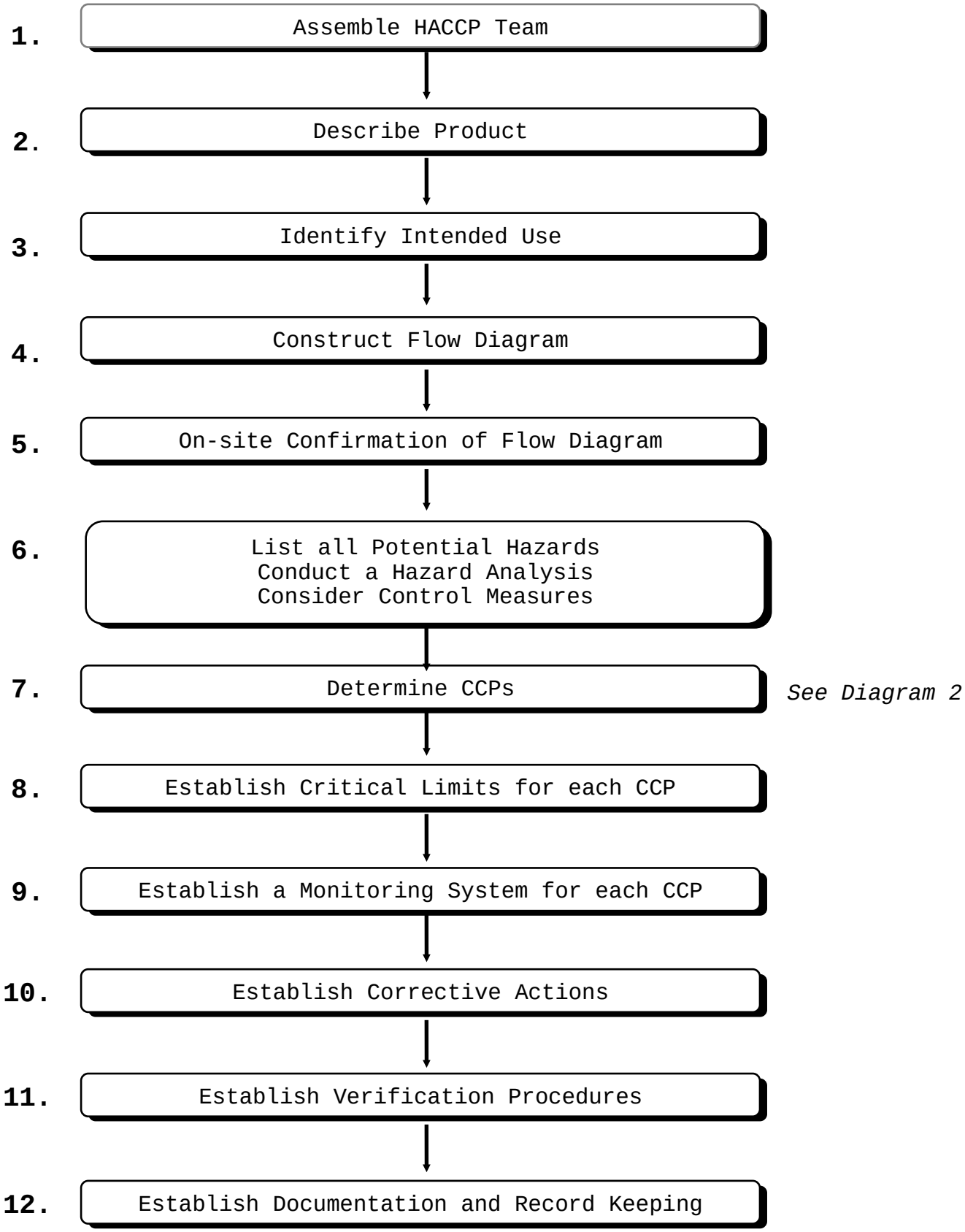
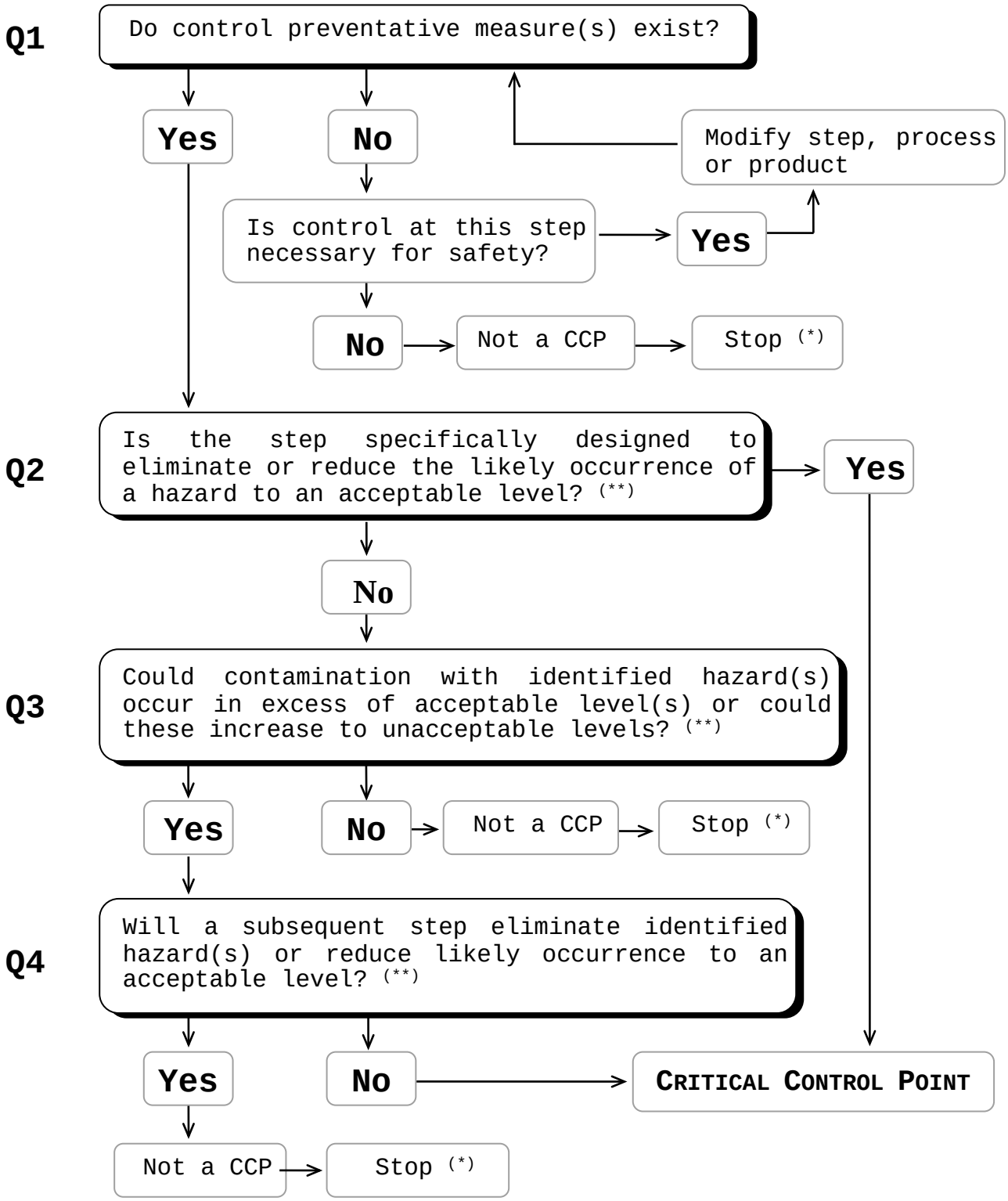


DIAGRAM 2

EXAMPLE OF DECISION TREE TO IDENTIFY CCPS
(ANSWER QUESTIONS IN SEQUENCE)



(*) Proceed to the next identified hazard in the described process.

(**) Acceptable and unacceptable levels need to be defined within the overall objectives in identifying the CCPs of HACCP plan.

DIAGRAM 3

EXAMPLE OF A HACCP WORKSHEET

1. Describe Product

2. Diagram Process Flow

3.

LIST							
Step	Hazard(s)	Control Measure(s)	CCPs	Critical Limit(s)	Monitoring Procedure(s)	Corrective Action(s)	Record(s)

4. Verification

From:	Drummond Food Science Advisory
To:	Morissette, Rachel
Subject:	Re: Questions for GRAS Notice No. GRN 000669
Date:	Monday, November 28, 2016 6:14:22 AM
Attachments:	GRN 669 FDA Response Qu 5 addition.pdf
Importance:	High

Dear Rachel

Further to the response forward last week please find attached the response to Qu 5.

Please let me know if there is any further information or clarification needed

Hoping you had a lovely Thanksgiving

With kindest regards
Lynley

Lynley Drummond
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> On 24/11/2016, at 1:29 AM, Drummond Food Science Advisory <lynley_dfsa@me.com> wrote:
>
> Dear Rachel
>
> Please find attached a letter of response to the questions raised in your letter of 8 November 2016.

Clean copies of specific sections have been provided as separate documents as it was rather cumbersome and awkward as a single document, however I appreciate this may not work for your purpose so would appreciate any further suggestions.

As you will note one of the key areas of Confidentiality has been addressed. Discussions with Synlait regarding the importance of transparency and availability of information have met with a positive response and significant changes to the status of much of the information in Part 7. I do hope this is useful.

With kind regards

Lynley

<Amended Pages>
<Appendix Pages Updates>
<GRN 669 FDA Response to Letter of 8 Nov _ 23 Nov 2016.pdf>

On 19/11/2016, at 1:34 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:

Lynley Drummond
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Dear Lynley,
A revised copy of the entire notice is not required and not preferable. Please provide point-by-point responses in a separate document, which will

serve as an amendment to the original notice. A clean copy of specific sections of the notice can be provided in the same document as the point-by-point responses. The original version of the notice is the one that appears on the FDA GRAS notice website, with the amendment available for request through FOIA. Hope this helps. Please let me know if you have further questions.

Best regards,

Rachel

Rachel Morissette, Ph.D.
Consumer Safety Officer
U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Biotechnology and GRAS Notice Review
5001 Campus Drive, HFS-255
College Park, MD 20740-3835
Email: Rachel.Morissette@fda.hhs.gov

From: Drummond Food Science Advisory [mailto:lynley_dfsa@me.com]
Sent: Thursday, November 17, 2016 9:11 PM
To: Morissette, Rachel
Subject: Re: Questions for GRAS Notice No. GRN 000669

Dear Rachel

As we are working through the reply to the questions raised in your letter of 08 Nov, I just wanted to check in with you regarding the structure of the reply. As some amendments to the Notice itself are required, the intent is to provide an updated version of the Notice, accompanied by a letter of explanation / guidance around the specific changes.
I would really appreciate your comment as to whether this is an acceptable way to resolve some of the points, or if this is not a preferred option, what would be.

With sincere thanks in advance

Best regards
Lynley

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On 10/11/2016, at 2:43 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:

Thanks!

Rachel

Rachel Morissette, Ph.D.
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Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Biotechnology and GRAS Notice Review
5001 Campus Drive, HFS-255
College Park, MD 20740-3835
Email: Rachel.Morissette@fda.hhs.gov

From: Drummond Food Science Advisory [mailto:lynley_dfsa@me.com]
Sent: Tuesday, November 08, 2016 4:55 PM
To: Morissette, Rachel
Subject: Re: Questions for GRAS Notice No. GRN 000669

Dear Rachel

Thank you for the questions raised, I acknowledge receipt and the 10 working day response time.

With sincere thanks

Lynley

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On 9/11/2016, at 7:57 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:

<11-8-16 GRN669 Questions for Notifier.pdf>

Drummond
Food Science Advisory Ltd

Dr. Rachel Morissette, Ph.D.
Consumer Safety Officer
U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety (OFAS)
Division of Biotechnology and GRAS Notice Review

27 November 2016

Dear Dr. Morissette

Further to my letter of 23 November addressing the questions outlined in your review of GRN 000669, please find below the response to question 5.

5. In the notice, Synlait states that by binding iron, cMDLF helps to inactivate potentially pathogenic bacteria. However, the iron-binding ability of cMDLF also raises the following issues:

a. It has been proposed, as well as experimentally demonstrated, that lactoferrin is a protein with antibacterial properties to some bacteria but not all. Citing the currently available published literature, please address how the selective antibacterial property of lactoferrin may be responsible for its ability to inhibit pathogenic bacteria but not probiotic bacteria. Likewise, please provide comment on the fact
that lactoferrin may not be able to inhibit all known pathogenic bacterial species and strains.

The antimicrobial properties of Lf are well established, and are achieved via a range of mechanisms; its ability to sequester iron which is indispensable for for the growth of micro-organism, direct interaction with microbial surfaces resulting in membrane damage and potential cell lysis, and inhibition of biofilm formation (Lingappan, Arunachalam, & Pammi, 2013; Oda, Wakabayashi, Yamauchi, & Abe, 2014). In a recent review addressing the potential role of bLf in the prevention of necrotizing enterocolitis (NEC) Sherman (2013) suggested the iron sequestering ability of bLf, originally hypothesized by Bullen, Rogers, and Leigh (1972) as the putative mechanism for the bacteriostatic effects of bLf observed on *E.coli,* although a recognised mechanism, is no longer considered the major anti-bacterial mechanism in the intestinal lumen. The bacteriostatic and bacteriostatic effects related to the ability of Lf to bind to a range of bacterial components (e.g. cell wall-associated lipopolysaccharide (LPS), flagellin and DNZ (CpG)) of a range of Gram-negative and Gram-positive bacteria (Legrand, 2016; Sherman, 2013). More recently Majka et al. (2016) also reported the LPS binding ability of bLf may play an important role in the prevention of neonatal sepsis. The formation of potent bactericidal peptides resulting from the digestion of Lf is also well documented (Bellamy, Takase, Wakabayashi, Kawase, & Tomita, 1992; Bellamy et al., 1993a; Bellamy et al., 1993b; Longhi, Conte, Bellamy, Seganti, & Valenti, 1994; Orsi, 2004). Lactoferricin susceptible organisms include *Escherichia coli, Salmonella enteritidis, Klebsiella pneumoniae, Proteus vulgaris, Yersinia enterocolitica, Pseudomonas aeruginosa, Campylobacter jejuni, Staphylococcus aureus, Streptococcus mutans, Corynebacterium diphtheriae, Listeria monocytogenes* and *(Bellamy et al., 1992)*. The

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known anti-bacterial activity of lactoferrin is limited to those species reported in the literature, and it is not believed to inhibit all known pathogenic bacterial species and strains.

In a 2009 review, Jenssen and Hancock (2009) identified and tabulated the activity and putative modes of action of Lf against a wide range of organisms (Table 1 shown below). Similarly Lingappan et al. (2013) reviewed the antimicrobial activities of Lf, tabulating effects and putative modes of action. The effects of Lf on enteric pathogens (*E. coli, Salmonella* & *Shigella*) was reviewed by Ochoa and Cleary (2009), who concluded the protection against gastroenteritis is a biologically relevant activity of Lf . Recently, Stecksen-Blicks, Granstrom, Silfverdal, and West (2015) reported a negative association of Lf levels in breastmilk with *Candida* colonisation of infants at 6 months of age. Iron acquisition by *Candida* is a factor contributing to its fitness and virulence, however Lf has not been described as a potential iron source but rather a potent inhibitor of *C. albicans* growth (Almeida, Wilson, & Hube, 2009).
Furthermore, the potential antibacterial properties of Lf may work synergistically with secretions from probiotic bacteria to restrict the growth of methicillin resistant *Staphylococcus aureus* (MRSA) (Chen, Jheng, Shyu, & Mao, 2013b), and in combination with lactoferrin-resistant probiotics against food-borne pathogens (Chen, Jheng, Shyu, & Mao, 2013a).

In contrast to the bacteriostatic and bactericidal properties of Lf, Lf is also known to promote the growth of probiotic bacteria. However this is conditional and should ideally be more properly recognised as “lactoferrin–resistant” probiotics, as Lf may inhibit, promote, or have no effect on the growth of probiotic bacteria (Chen et al., 2013a; Chen, Ku, & Chu, 2014; Tian, Maddox, Ferguson, & Shu, 2010). Petschow, Talbott, and Batema (1999) demonstrated that the ability of Lf to promote the growth of Bifidobacterium spp. *in vitro* is independent of the iron saturation level for Lf and suggest that binding of Lf to bifidobacteria cells may be involved but is not sufficient for stimulation of bifidobacteria growth.
Chen et al. (2014) observed that 2 probiotic strains (*Lactobacillus acidophilus* and *L. rhamnosus* (ATCC 7469) were more resistant to the antibacterial activity of bLf than other probiotics, whose growth rates were inhibited by bLf in a dose-dependent manner. Most importantly Chen et al. (2014) concluded that given the minimum inhibitory concentrations (MIC) needed to retard the growth of probiotics, that bLf possesses stronger anti-bacterial activity against pathogens than against probiotic bacteria, and so it remained a useful adjunct to formulations containing probiotics.

Biological activity of lactoferrin

Activity	Target	Mode of action
Gram-positive bacteria	*S. mutans*	Iron-independent interaction with bacterial cell surface
	S. epidermidis	Interaction with lipoteichoic acid on bacterial surface
	S. epidermidis	Prevents biofilm formation – probably through iron sequestering
Gram-negative bacteria	*E. coli*, *S. typhimurium*	Cation chelators, damaging the bacterial membrane, altering the outer membrane permeability, resulting in a release of LPS
	H. influenzae	Altering bacterial virulence – degrading IgA1 and Hap
	S. flexneri	Disrupt bacterial type III secretion system – degrading IpaB and IpaC
	E. coli	Disrupt bacterial type III secretion system – degrading EspA, EspB and EspC
	S. typhimurium	Interaction with the bacterial surface
	P. aeruginosa	Prevents biofilm formation – probably through iron sequestering
	B. cepacia	Prevents biofilm formation – probably through iron sequestering
	B. cenocepacia	Prevents biofilm formation – probably through iron sequestering
Enveloped viruses	HSV	Targets adsorption/entry – contradicting results whether there is a direct effect on the viral particle or not
	HCMV	Targets adsorption/entry – no effect on the viral particle
	VSV	Upregulation of machrophage interferon α/β expression
	Hepatitis B	Targets cellular molecules interfering with viral attachment/entry
	Hepatitis C	Targets viral envelope protein E1 and E2 – blocks entry
	Hepatitis G	Unknown
	HIV	Targets V3 loop in envelope protein gp120 – blocks CXCR4- or CCR5-attachment
	Feline herpes virus-1	Targets viral attachment/entry
	Sindbis virus	Targets adsorption/entry – no effect on the viral particle
	Semliki Forest virus	Targets adsorption/entry – no effect on the viral particle
	RS-virus	Unknown
	Hantavirus	Targets adsorption/entry (not heparan sulphate) – no effect on the viral particle
Naked viruses	Rotavirus	Viral interaction – prevents hemaglutination and attachment to cellular receptors
	Poliovirus	Targets viral adsorption/competes for viral receptor interaction
	Adenovirus	Targets viral adsorption/binds viral protein III and IIIa.
	Enterovirus (EV71 and Echovirus 6)	Targets viral adsorption – binds both cellular receptors and the viral surface protein VP1. Inhibits apoptosis
Yeast and fungi	*C. albicans*, *C. tropicalis*, *C. krusei*, *C. guilliermondii*, *C. parapsilosis*, *C. glabrat*	Cell wall perturbation
	A. fumigatus	Iron sequestering
Parasites and other eukaryotic microbes	*P. berghei*	Targets host cell entry
	P. carinii	Iron sequestration
	E. histolytica	Probably linked to iron sequestration
	B. caballi	Iron sequestration
	B. equi	

Table 1: Biological activity of lactoferrin (from Jenssen and Hancock (2009))

The mechanisms by which bLf appears to differentiate bacteriostatic or bactericidal activity against probiotics is not clearly defined, as the modes of action are complex. Oda et al. (2014) reviewed the effects and possible mechanisms of Lf on bifidobacteria:

- Iron saturation: The antimicrobial effects of Lf against Bifidobacteria have mainly been observed under iron-restricted conditions. If inadequate iron levels are present, for bifidobacteria growth, the addition of iron-unsaturated Lf would further decrease the levels of iron available for Bifidobacteria, hence inhibiting growth. In contrast if adequate levels of iron are present, the iron-saturation status of the Lf does not have a marked effect on the growth of bifidobacteria. The bifidogenic activity of apo-Lf or <10% iron-saturated Lf is due to mechanisms other than the donation of iron.
- The sugar chains attached to Lf could be a potential carbon source used by bifidobacteria for growth
- Lf peptides generated during digestion may also stimulate growth of bifidobacteria. Lactoferricin, a known potent antimicrobial peptide has only a week effect against bifidobacteria (Bellamy et al., 1992). Bifidobacteria may recognizes disulphide bonds in peptides, which may be important for cancelling antimicrobial activity or exerting bifidogenic activity. The peptide sequence itself may be important for bifidogenic activity
- Evidence to suggest a consistent relationship between the binding of Lf or its peptides to bLf-binding proteins is insufficient to explain its bifidogenic mechanism

- Lf may work in synergy with other components of milk to stimulate bifidobacteria growth.

Overall Oda et al. (2014) concluded that Lf may be partly responsible for the formation of a bifidus flora in infants by inhibition of pathogenic bacteria, and the promotion of bifidobacteria growth. The proposed that Lf peptides may be the bifidogenic active principle of Lf and the effect is also the result from synergy with other milk components, at least in breast-fed infants.

From a clinical perspective, although many of the earlier studies in infants on the effects of bLf added to formula were intended to look at the effects on fecal microflora, generally results showed little effect, and none of the studies were designed to determine the effect on pathogenic bacteria (Ochoa, Pezo, Cruz, Chea-Woo, & Cleary, 2012). A high dose of bLf (100mg/100ml) was able to establish a bifidus dominant flora, but only in half of the infants and only at 3 months (Ochoa et al., 2012; Roberts et al., 1992).

b. It is well-known that the iron level in adults is very tightly regulated through the participation of various proteins starting from the iron uptake in the intestine by the DMT1 transporter. In contrast, in neonates, iron absorption is generally greater and lactoferrin may play a role. Citing the currently available published literature, please address why the iron-binding property of lactoferrin is not a safety concern in terms of adverse effect on the iron status in the infant.

Early studies on the effects on iron status in infants fed bLf supplemented formula typically showed no effect (neither beneficial nor deleterious) (Ochoa et al., 2012). Only in the study by Chierici, Sawatzki, Tamisari, Volpato, and Vigi (1992) infants receiving the higher dose of bLf (100mg / 100 ml) had significantly higher serum ferritin levels at days 90 and 150. In a study comparing Lf-free breast milk with normal breast-milk Davidsson, Kastenmayer, Yuen, Lönnerdal, and Hurrell (1994) observed that iron absorption was significantly lower in the breast-milk fed group than in the Lf-free breastmilk fed group. That study suggested Lf does not have a role in the enhancement of iron availability in infants (Ochoa et al., 2012). This is supported by the work of Ward, Mendoza-Meneses, Cunningham, and Conneely (2003) who showed using lactoferrin knockout mice and Lf ablation, that Lf is not essential for iron delivery to the neonate, however that it may have a role in iron homeostasis via sequestration and inhibition of excess iron uptake in the suckling period to prevent iron induced cellular oxidative damage, together with controlling pathogens in the intestinal lumen (Ward, Paz, & Conneely, 2005). In a study investigating the relationship between iron status and breast-milk lactoferrin levels no correlation was observed at either 6 weeks or 6 months of age (Mehta, Faridi, Sharma, Singh, & Sharma, 2016)

A recent study in 213 previously breast-fed infants who received either a control or lactoferrin supplemented formula (38 mg bLf/ 100ml) reported a beneficial role of bLf on iron status with significantly higher calculated total body iron content (TBIC), and iron absorption in the small intestine (as determined by the improved TBIC and TFR-index measures) (Chen et al., 2015)

In a piglet study (Shan, Wang, Wang, Liu, & Xu, 2007) the iron status of piglets fed control, antibiotic supplemented or bLf supplemented formula was determined on day 15 and 30. Lactoferrin supplementation increased serum iron values by 22% ($P < 0.05$) on day 15 and by 23% ($P < 0.01$) on day 30compared to the control group, but did not affect serum total iron-binding capacity at either time point. There was no difference between the antibiotic treated group and the bLf treated group (Shan et al., 2007).

The role of Lf in iron homeostasis may be limited to the early postnatal period, where Lf receptors in the small intestine of neonates take up iron from Lf into cells and presumably exert other physiological functions (Suzuki, Lopez, & Lönnerdal, 2005).

The seemingly duplicitous role of Lf in iron homeostasis has been eloquently reviewed by Collard (2009), who identified that although the major iron- transport proteins of relevance of the new-born are DMT-1 and ferroportin, the putative role of lactoferrin is remains (Figure 1 form (Collard, 2009)).

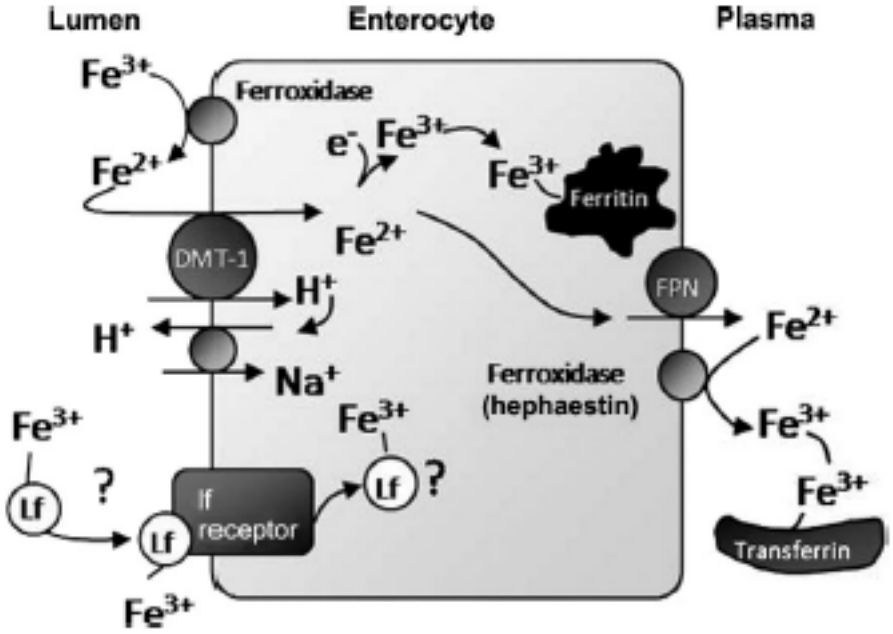

FIGURE 1

The known and postulated iron-transport processes believed to be operating in the neonatal duodenum. The well-accepted processes are shown in the upper part of the diagram. Dietary iron is converted to Fe^{2+} by ferroxidase enzymes to enable it to be transported into the enterocyte by DMT-1. Within the enterocyte the iron remains within the enterocyte (mostly bound to ferritin) or transported out by ferroportin (FPN). The transported iron is then converted to Fe^{3+} by hephaestin to allow it to bind to transferrin. The proposed, but currently unproven, transport system is shown in the lower part of the diagram. In this process, iron bound to lactoferrin (Lf) is transported into the enterocyte via the lactoferrin receptor. The question marks indicate the unproven nature of the process and the lack of knowledge concerning the fate of the iron entering the entero-cyte by this route.

Whilst Lf is able to bind free iron and consequently limit the absorption of dietary iron and reduce the incidence of iron-induced oxidative stress, in addition to acting as an iron chelator in the gut, lactoferrin has also been proposed as a means of transporting iron from the gut in neonatal mice via the lactoferrin receptor present on the apical border of enterocytes (Collard, 2009; Lopez, Suzuki, & Lönnerdal, 2006). This transport mechanism, which seems to be responsive to iron needs, could potentially help to limit the influence of dietary iron deficiency during the period in which DMT-1 is poorly responsive to iron requirement. However, lactoferrin seems to enhance iron absorption in newborn calves only when fully saturated with iron (Collard, 2009; Kume &

Tanabe, 1996); this would be unlikely to occur if luminal iron level was low. Also, neonatal mice rendered lactoferrin deficient by knocking out the gene that expresses lactoferrin showed no evidence of reduced intestinal iron uptake (Collard, 2009; Ward et al., 2003), and transgenic mice overproducing lactoferrin did not increase the hemoglobin levels in their suckling neonates except at very high maternal dietary iron intake (Collard, 2009; Hanson et al., 2001), thus not supporting the hypothesis that lactoferrin functions as an intestinal iron scavenger, at least at high doses (Hanson et al., 2001). It is possible that lactoferrin acts mainly as an iron chelator in neonatal gut but when fully saturated with iron it may contribute to gut iron transport. Unlike the situation in the gut, liver DMT1 gene expression in early infancy has been shown to increase with iron deficiency and decrease during iron loading, suggesting that the liver may play an important role as a sink or source for use in regulating iron metabolism during early infancy when gut transport may be unresponsive (Collard, 2009; Leong, Bowlus, Tallkvist, & Lonnerdal, 2003).

More recently Lönnerdal (2016), postulated in addition, that the potential of lactoferrin to stimulate cell proliferation and differentiation may contribute to the development of the intestinal mucosa of infants. Increased mucosal development caused by lactoferrin, may, therefore, increase the mucosal surface and enhance the uptake of iron and other nutrients (Lönnerdal, 2016).

From a clinical perspective, no adverse or safety concerns (including particular issues on iron status) have been reported in studies of bLf fortified formula in infants. There is no evidence to suggest that the presence of bLf in formula has an adverse effect on the iron status of neonates, nor that the iron sequestering potential of bLF specifically has a negative effect on iron status.

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Please do not hesitate to request further details or clarification. We appreciate the opportunity to respond to your questions and will welcome further dialogue as required

Yours sincerely

Lynley N Drummond

From:	Drummond Food Science Advisory
To:	Morissette, Rachel
Subject:	Response to recent questions
Date:	Sunday, December 18, 2016 8:53:15 PM
Attachments:	GRN 669 FDA Response_Chem Review Questions.docx GRN 669 Page 18 amended 19 Dec 2016.pdf
Importance:	High

Dear Rachel

My apologies for the minor delay in reply to these questions - my travel schedule leading up to Christmas has been ridiculous and I left several files behind on the last sojourn.

Please find attached a letter that contains the information relating to bLf levels in the various formats and confirms the typo identified in your email of Dec 14

My very best wishes for a lovely Christmas and New Year

With kindest regards
Lynley

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Division of Biotechnology and GRAS Notice Review

19 December 2016

Dear Dr. Morissette

1. Clarification on Usage Rates of Bovine Lactoferrin in Liquid RTF and Concentrated Formula

Background:
The rational for intended use of bLf on a solids basis as submitted in GRN 669 was to provide some flexibility for companies intending to use the bLf in a range of products (powders, liquids RTF and concentrates) based on formulation preferences and techniques. Formulation is often completed on a solids basis, to balance the delivery of nutrients and energy to meet the requirements of infants. A solids basis provides a common baseline of composition across format (powder, RTF or concentrate) ranges for a given product. There is no set rule for absolute values of reconstitution rates and solids concentrations of formula however the energy and nutrient requirements of infants do mean there is a relatively narrow window for the solids content of the various formula formats. Typically, the reconstitution rates of powder products result in formula with similar solids levels of RTF products. Concentrated products require a 1:1 dilution prior to feeding, hence the solids levels are normally twice that of RTF.

Predicted bLf content of formula types and formats:
The following table reflects typical solids and reconstitution rates for formula across the different age ranges and by product format type. Toddler milks are not typically available in concentrate format, however if in the future such products were to be placed on the market it would be expected the dilution rate would also be 1: 1 and therefore the solids level double that of the RTF or reconstituted powder equivalent.

Summary of the Infant Formula and Use-Levels for Bovine Lactoferrin in the U.S.			
Formula Type	**Formula Format**	**Typical Solids Content (%w/v)****	**Proposed bLF Level (mg/100 mL)**
Formulas for Infants 0 to 6 months	Powder	**12.5** -13.0	12.5 -13.0
	RTF	**12.5** - 13.0	12.5- 13.0
	Concentrate	25-26	25-26
Formulas for Infants 7 to 12 months	Powder	**13.5** -14.0	13.5 – 14.0
	RTF	**13.5** -14.0	13.5 – 14.0
	Concentrate	27-28	27-28
Formulas for Toddlers 13 to 36 months	Powder	14-**15**	14-15
	RTF	14-**15**	14-15

** note the bolded values are those that Synlait nominated as representative solids levels in GRN 669

2. Correction of CFR reference regarding personal Privacy information

Apologies, that does appear to be a typo, and the corrected amended page accompanies this letter.

Please do not hesitate to request further details or clarification. We appreciate the opportunity to respond to your questions and will welcome further dialogue as required

Yours sincerely

Lynley N Drummond

1.7 AVAILABILITY OF INFORMATION

The data and information that are the basis for Synlait's conclusion of the GRAS status of bLf under the intended conditions of use are available for the FDA's review, both during or after the evaluation of this Notice. Upon request, a complete copy of the data and information will be provided to the FDA either in an electronic format that is accessible for FDA evaluation, or on paper. Upon request, the data and information are available for the FDA to review and copy during customary business hours at either of the following addresses:

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Synlait acknowledges this Notice contains personal privacy information relating to individuals who have prepared and are responsible for this Notice, and that these individuals are aware of this disclosure and the implications under 21 CFR § 20.

Synlait has identified Confidential and not generally available and personal privacy information relating to members of the GRAS Panel that is presented in Part 7: Appendix 6 which it considers are exempt from disclosure under the Freedom of Information Act, 5 U.S.C. §552. Synlait has not identified any trade secrets included as a part of this Notice and authorizes for all information within this Notice to be provided to the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture, as required.