Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Internal use only

Food-therapeutic good interface product assessment

Overview

Product	Souvenaid
Source	Referred to CRP by s22 [redacted] on 13/05/2013
Details	Enquiry via News on 15/05/2013 in response to a complaint from s22 [redacted].

Assessment against Food-Therapeutic Goods guidance tool

Question	Assessment outcome
Q1 - Oral use?	Yes
Q2 - s7 declaration	No
Q3 - s7AA declaration	No
Q4 - goods for which there is a food std?	?? 2.9.5: Food for special medical purposes ??2.6.2: non-alcoholic beverages & brewed soft drinks.
Q5 - tradition of use	Q5(a) – What kind of goods is the thing? Water with added vitamins & minerals. Q5(b) – What is the form in which the thing is presented? Flavoured drink (vanilla or strawberry) 125ml Q5(c) – Is there a use of the goods as "food for humans" in Aus/NZ in that form? Yes Q5(d) – Is there a tradition of that use in Aus/NZ? No
Q6 - meets TG definition (a)	Q6(a) – represented to be for therapeutic use? Yes Q6(b) – likely to be taken to be for therapeutic use because of the way in which it is

Question	Assessment outcome
	presented? Yes Q6(c) – likely to be taken to be for therapeutic use for any other reason? Yes- claims in the promotional material
Q7 - meets TG definition (b)	?? No ?? Yes
Q8 – biological or device	No

Expert advice

Source	
State/Territory Health	
Internal working group	Overall impression: probably captured under FSANZ standard 2.9.5
Other expert (s)	

Outcome

Outcome	Food X	Medicine ☐	
Assessor	s22 [redacted]	Date	29/08/2013

Comments

s22 to communicate with s22 NSW Food Authority regarding the progress of their investigation: Contacted on 29/08/2013: "Dear s22

Thanks for your email. We are investigating the compliance of this product with the new standard under the Food Standards Code Standard 2.9.5 – Food for Special Medical Purposes. The product is represented for sale as a food under that standard.

We will soon finalise our investigation to determine whether the product and the various modes of advertising is indeed compliant with this Standard 2.9.5.

I am not in the office tomorrow but please call me on my direct line at any other time.

Kind regards

s22

s22
NSW Food Authority
safer food, clearer choices
6 Avenue of the Americas Newington NSW 2127 | PO Box 6682 Silverwater NSW 1811
Switch +61 2 9741 4777 | Helpline 1300 552 406 | www.foodauthority.nsw.gov.au
Direct line s22 | Fax +61 2 9741 4888 | Mob s22
s22 @foodauthority.nsw.gov.au

I have requested to be kept informed of progress made & of the eventual outcome.

Relevant definitions

Term	Source	Definition
		<as add required>

Examples of presentations

<as add required>

From: s22 @dhhs.vic.gov.au
To: s22
Cc: s22 ; s22 ; Francis, Jenny; s22 @dhhs.vic.gov.au; s22 @dhhs.vic.gov.au
Subject: RE: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]
Date: Wednesday, 9 January 2019 9:39:29 AM
Attachments: Neurofolin opinion s22 docx

Thank you s22 we will call you on that number at 3pm.

I have attached an email from an external expert in the Food Standards Code, s22 , who provides his opinion on Neurofolin as an FSMP.

Here is a link to the original proposal documents for the development of Standard 2.9.5, Foods for Special Medical Purposes, should you wish to look at these. Unfortunately there was a strong focus the products intended to be captured by the Standard and very little overt discussion on those that shouldn't:
http://www.foodstandards.gov.au/code/proposals/Pages/proposalp242foodsforspecialmedicalpurposes/index.aspx

Kind regards
s22

s22 | s22 | **Food Policy**
Food Safety | Health Protection Branch | Department of Health and Human Services

50 Lonsdale Street, Melbourne, Victoria 3000
s22 @dhhs.vic.gov.au | p. s22
Please note my work days are Monday - Thursday

From: s22 " <s22 @health.gov.au>
To: s22 @dhhs.vic.gov.au" s22 @dhhs.vic.gov.au>,
Cc: s22 @health.gov.au>, s22 @health.gov.au>, "Francis, Jenny" <Jenny.Francis@health.gov.au>, s22 @dhhs.vic.gov.au" <s22 @dhhs.vic.gov.au>, s22 @dhhs.vic.gov.au" <s22 @dhhs.vic.gov.au>
Date: 09/01/2019 08:31 AM
Subject: RE: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

Hi s22

We will all be in Jenny Francis's office s22

Also do you have any documents that we should read prior to our teleconference.

Thanks s22

s22
s22
Regulatory Compliance Section
Regulatory, Education and Compliance Branch

Phone: s22
Mobile: s22
Email: s22 @health.gov.au

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
www.tga.gov.au

From: s22 @dhhs.vic.gov.au [mailto s22 @dhhs.vic.gov.au]
Sent: Tuesday, 8 January 2019 5:56 PM
To: s22
Cc: s22 ; s22 ; Francis, Jenny; s22 @dhhs.vic.gov.au; s22 @dhhs.vic.gov.au

Subject: RE: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

Thanks s22 Let's lock in 3 pm.
Let me know how you would like to dial in. I can provide a teleconference link if required.
s22

s22 | s22 | **Food Policy**
Food Safety | Health Protection Branch | Department of Health and Human Services

50 Lonsdale Street, Melbourne, Victoria 3000
s22 @dhhs.vic.gov.au | p. s22
Please note my work days are Monday - Thursday

From:	s22 @health.gov.au>
To:	s22 @dhhs.vic.gov.au" <s22 @dhhs.vic.gov.au>,
Cc:	s22 @health.gov.au>, s22 @health.gov.au>, "Francis, Jenny" <Jenny.Francis@health.gov.au>, s22 @dhhs.vic.gov.au" s22 @dhhs.vic.gov.au>, s22 @dhhs.vic.gov.au" <s22 @dhhs.vic.gov.au>
Date:	08/01/2019 05:48 PM
Subject:	RE: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

Hi s22
Tomorrow (Wednesday) afternoon would be good. Please advise a time and I will get it set up.

Thanks s22

Sent with BlackBerry Work
(www.blackberry.com)

From: s22 @dhhs vic gov au <s22 @dhhs vic gov au>
Date: Tuesday, 08 Jan 2019, 3:59 pm
To: s22 @health gov au>
Cc: s22 @health gov au>, s22 @health gov au>, Francis, Jenny <Jenny Francis@health gov au>, s22 @dhhs vic gov au s22 @dhhs vic gov au>, s22 @dhhs vic gov au s22 @dhhs vic gov au>
Subject: RE: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

Dear s22

Thank you for forwarding the information from Grunbiotics, together with their legal opinion.

We met with Grunbiotics in December and considered the information they provided together with an external expert opinion (an expert in the Food Standards Code). Our preliminary opinion was that Neurofolin is a therapeutic good and not a food for special medical purposes. We have since also sought an opinion from our legal services and a discussion with you at this point would be helpful to forming a final position on this.

s22 and s22 will join me. We have availability tomorrow afternoon, but then not again until next week.
Let me know what suits.
Kind regards
s22

s22 | s22 | **Food Policy**
Food Safety | Health Protection Branch | Department of Health and Human Services

50 Lonsdale Street, Melbourne, Victoria 3000
s22 @dhhs.vic.gov.au | p. s22
Please note my work days are Monday - Thursday

From:	s22 @health.gov.au>
To:	s22 @dhhs.vic.gov.au" s22 @dhhs.vic.gov.au>,
Cc:	"Francis, Jenny" <Jenny.Francis@health.gov.au>, s22 @health.gov.au>, s22 @health.gov.au>
Date:	08/01/2019 03:28 PM
Subject:	RE: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

Good afternoon s22

I have been advised you are now handling the Grunbiotics matter.

Would you be in a position to have a teleconference to discuss this matter further.

The following people from the TGA would be participants in the teleconference;
Jenny Francis- Principal Legal Advisor
s22
s22 complementary medicines
Myself

Kind regards,

s22

s22
s22
Regulatory Compliance Section
Regulatory, Education and Compliance Branch

Phone: s22
Mobile: s22
Email: s22 @health.gov.au

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
www.tga.gov.au

From: s22 @dhhs.vic.gov.au [mailto:s22 @dhhs.vic.gov.au]
Sent: Tuesday, 8 January 2019 3:00 PM
To: s22
Cc: s22 @dhhs.vic.gov.au
Subject: RE: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

Dear s22

I write to confirm receipt of the email below and subsequent attachments.

The documents have been forwarded on to s22 who has been handling this issue.

Kind regards,

s22 | Food Safety Science Officer
Food Safety Unit | Health Protection Branch
Department of Health and Human Services | 50 Lonsdale Street Melbourne Victoria 3000
p. s22 | e s22 @dhhs.vic.gov.au
w. www.health.vic.gov.au/foodsafety

From:	s22 @health.gov.au>
To:	s22 @dhhs.vic.gov.au"s22 @dhhs.vic.gov.au>,
Date:	08/01/2019 12:41 PM
Subject:	RE: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

SENSITIVE: LEGAL

Hi s22

My name is s22 I was a participant in the below teleconference and I am now in charge of the Grunbiotics matter for the TGA.

I would like to update the VIC Food authority with the information that the company has now supplied to have the product Neurofolin considered as a Food for special medical purposes. The company has agreed to the TGA supplying this information.

I have attached the three documents and would ask could you please review. The TGA would like to discuss this matter with VIC food authority prior to us meeting with Grunbiotics.

Kind regards,

s22

s22
s22
Regulatory Compliance Section
Regulatory, Education and Compliance Branch

Phone: s22
Mobile: s22
Email s22 @health.gov.au

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
www.tga.gov.au

From: s22 @dhhs.vic.gov.au [mailto:s22 @dhhs.vic.gov.au]
Sent: Wednesday, 25 July 2018 12:37 PM
Subject: Re: Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

Hi s22

Still up for meeting at 9.30am on s22

s22 | Food Safety Science Officer
Food Safety Unit | Health Protection Branch
Department of Health and Human Services | 50 Lonsdale Street Melbourne Victoria 3000
p. s22 | e. s22 @dhhs.vic.gov.au
w. www.health.vic.gov.au/foodsafety

VICTORIA State Government | Health and Human Services

Update: Neurofolin - Grunbiotics [SEC=UNCLASSIFIED]

Thu 26/07/2018 9:30 AM - 10 00 AM

Attendance is required for s22

Chair s22 @health.gov.au

Location Teleconference

s22 @health.gov.au has sent updated information

Required s22 /HeadOffice/DHS, s22 @health.gov.au,

Hi s22

As discussed, Grunbiotics is available on Thursday morning at 9 30am for a teleconference. I will dial everyone into the call. Is the best number to dial you in 9096 5510?

The following staff members from Grunbiotics/Mylan will be included in the teleconference on Thursday:

s22 Grunbiotics
s22 Grunbiotics; and
s22 Mylan (distributor)

Below is he email correspondence for your reference, which includes the ini ial email to Grunbiotics, and their response. This correspondence only relates to the product Neurofolin (http://www.grunbiotics.com/neurofolin-for-depression/)

Thanks again for your input,
s22

Dear s22

Thank you for your time on the phone wi h regards to the product Neurofolin.

After consultation with our Complementary Medicines Branch at the TGA, it has been determined that this product does not meet the definition of food for special medical purposes for the following reasons:

- this product is not intended for exclusive or partial feeding; and
- depression does not cause a limited or impaired ability to take, digest, absorb, metabolise or excrete L-methylfolate.

Please see excerpt from the Food Standard Australia New Zealand Act 1991:

'food for special medical purpose' means a food that is: (emphasis added)
(a) specially formulated for the dietary management of individuals:
(i) by way of exclusive or partial feeding, who have special medically determined nutrient requirements or whose capacity is limited or mpaired to take, digest, absorb, metabolise or excrete ordinary food or certain nutrients in ordinary food; and
(ii) whose dietary management cannot be completely achieved without the use of the food; and
(b) intended to be used under medical supervision; and
(c) represented as being:
(i) a food for special medical purposes; or
(ii) for the dietary management of a disease, disorder or medical condition.

In addi ion, it has been determined that the product meets the definition of a therapeutic good for the following reasons:

- based on the statements on the website, the goods, including presentation, meet the definition of therapeutic use since references are made to curing or alleviating a disease, ailment, defect or injury in persons and influencing, inhibiting or modifying a physiological process in persons.

Please see excerpt from the Therapeutic Goods Act 1989:

The definition of 'therapeu ic use' in subsection 3(1) of the Act states that (emphasis added):
therapeutic use means use in or in connection with:
(a) preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury in persons; or
(b) influencing, inhibiting or modifying a physiological process in persons; or
(c) testing the susceptibility of persons to a disease or ailment; or
(d) influencing, controlling or preventing conception in persons; or
(e) testing for pregnancy in persons; or
(f) the replacement or modifica ion of parts of the anatomy in persons.

As such, if you intend on manufacturing, advertising and supplying this product, you must have the product entered onto the Australian Register of Therapeutic Goods<https://www.tga.gov.au/australian-register-therapeutic-goods>.

Here is some information for you: https://www.tga.gov.au/overview-supplying-therapeutic-goods-australia

Can you please advise on how you would like to proceed wi h this matter?

Kind regards

s22 [redacted]
Regulatory Compliance and Support Section
Regulatory Practice, Education and Compliance Branch

Phone: s22 [redacted]
Email: s22 [redacted]@health.gov.au<mailto:s22 [redacted]@health.gov.au>

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
www.tga.gov.au

Dear s22 [redacted]
Thank you for your email of 15 June giving us the opportunity to provide you with a response to your request for information by Friday 29 June.
At the outset, I wanted to thank you for the positive and constructive approach you have taken to engaging with us about these issues. Compliance with applicable laws and standards is a core value of Grunbio ics. We have carefully reviewed all he issues raised in your emails. We set out in this reply an overview as to the approach that we have taken in developing Neurofolin, and the approach we propose to take with respect to the marketing of the product to satisfy the TGA's concerns, including, where necessary, re-framing some of the claims we make about Neurofolin.

Food for Special Medical Purposes
Following FSANZ standard 2.9.5: A Food for Special Medical Purposes (FSMP) means a food that is specially formulated for the dietary management of individuals " … who have special medically determined nutrient requirements or whose capacity is limited or impaired to take, digest, absorb, metabolise or excrete ordinary food or certain nutrients in ordinary food." (the bolded words are relevant to the disease state of Major Depressive Disorder ("depression"), and the need for dietary management with a FSMP).
Neurofolin is a food for special medical purposes. Scientific, medical and regulatory experts were extensively consulted ahead of launching the product in Australia to ensure it met the definition of a FSMP. The TGA's "Food-Medicine Interface Guidance Tool" was carefully used as part of this review, with expert guidance to ensure correct interpretation. We are constantly assessing our compliance with the relevant regulatory frameworks, and have always been conservative in our approach. After receipt of your query we undertook an ad-hoc review and have confirmed Neurofolin con inues to meet the definition of a FSMP.
Neurofolin is specifically formulated for the partial feeding of patients diagnosed with depression. L-methylfolate when required for the effective dietary management of some individuals diagnosed with depression exceeds what may be reasonably obtained from sources that are not FSMPs. Moreover, a specific FSMP is necessary to address an underlying metabolic impairment typical in individuals with

depression.
Exclusive or partial feeding
Neurofolin is intended for partial feeding. Neurofolin is a nutritionally incomplete food product with a nutrient-adapted formulation specific for a disease, disorder or medical condition which is not suitable to be used as the sole source of nourishment.
The ingredients in Neurofolin are all food ingredients:

- Food acid as citric acid
- Mineral salts as sodium bicarbonate and sodium carbonate
- Sweetener as glucose syrup (rice)
- Inulin (from chicory)
- Natural flavour as grapefruit extract
- Sweetener as sucralose
- Vegetable gum as xanthan gum
- Natural colour as safflower extract
- Vitamins as L-methylfolate calcium and cyanocobalamin

Depression and medically determined nutrient requirements
The relationship between depression and folate deficiency has been under investigation for over half a century, with scientific publications noting he link from circa 1970. Population and cohort studies from around the world have found that many patients with a diagnosis of depression had significantly lower levels of serum folate level compared to healthy individuals. While some other large scale studies have found only condi ional significant relationships between folate intake and depression symptoms (such as only in men, although other studies find that women also experience this link), hese studies do not measure actual blood or cerebral folate levels, only dietary folate intake. Due to established inborn errors of metabolism described below, this is an inappropriate measure as it does not reflect the heterogeneity of the popula ion. Supporting this, a recent study that found that in a population of treatment resistant depression patients, cerebral folate levels could remain low even when serum folate levels remained normal. More focused clinical studies have likewise found that approximately one third of patients with a depression diagnosis display a serum folate deficiency. Meta-analyses have also confirmed the link between low folate evels and depression.
It should be noted, that the key focus should remain cerebral folate levels, as the mechanism of action that folate influences depression occurs at a neurological level, it requires folate to be metabolised, so it may pass he blood brain barrier. Overall, despite inconsistencies in the methods used in research papers, the finding that depression diagnosed patients show a deficiency in folate levels has been replicated sufficiently to highlight the need for a FSMP that can address the medically determined nutrient requirement of these patients.
Depression and metabolic impairment
Patients diagnosed with depression commonly have an impaired capacity to metabolize folate as found in ordinary food. Some gene ics studies suggest that up to 70% of patients with depression have an inborn error of metabolism, exhibiting a genetic abnormality as a carrier of the MTHFR 677T allele, showing either a C677T heterogeneous or homogenous polymorphism. This gene is implicated in the ability to convert regular dietary folate, including folic acid, to L-5-methyltetrahydrofolate ("L-methylfolate", "L-5-MTHF"). These patients show a markedly reduced ability to metabolise folate to L-5-MTHF, a feature not able to be remedied by intake of normal food. Without the ability to metabolise folate to L-5-MTHF, it cannot be absorbed into the central nervous system for the adequate synthesis of monoamine neurotransmitters. This can lead to a functional alteration to the metabolic processing of folate to L-5-MTHF, resulting in a deficiency of L-5-MTHF which can only be addressed through dietary management provided by a FSMP such as Neurofolin.
If you would like the references for these statements, we are able to provide them.

Claims
We have carefully reviewed each of the claims in issue. Below we set out the proposed rewording of each claim that the TGA has identified, to address the TGA's concerns and ensure that the product is not seen to be being marketed as a therapeutic good:
Existing claim Comment Proposed claim
Neurofolin contains L-methylfolate, an active form of folate that addresses part of a complex deficiency found in people with depression.
This statement was not intended to contain a herapeutic claim, but rather to address the requirements in Standard 2.9.5-10(c) and (d), ndicating the medical purpose of the food, and/or describing the characteristics that make it appropriate for a medical purpose.
Neurofolin contains L-methylfolate, an active form of folate that addresses part of a complex deficiency found in people with depression. Unlike synthe ic folic acid, L-methylfolate effectively crosses the blood-brain barrier to contribute to the synthesis of mood regulating neurotransmitters like serotonin and dopamine. This statement was not intended as a therapeutic claim, but rather to draw a parallel with the permitted general level health claims for folate (ie, that it contributes to normal psychological func ion). General level heal h claims are not therapeutic claims.
This statement was included to address he requirements in Standard 2.9.5-10(c) and (d), indicating the medical purpose of the food, and/or describing the characteristics that make it appropriate for a medical purpose. Neurofolin contains an active form of folate to help nutritionally support normal psychological function. Unlike synthetic folic acid, which may not be absorbed properly by people with depression, Neurofolin is specifically formulated to help the natural mood regulating processes in the brain.
Neurofolin is a food for special medical purposes for the dietary support of depression management. It contains 15mg of L-methylfolate, a form of folate that helps support the production of mood-regulating brain chemicals such as serotonin and noradrenaline. This statement was not intended to contain a therapeutic claim, but rather to address the requirements in Standard 2.9.5-10(c) and (d), indicating the medical purpose of the food, and/or describing the characteris ics that make it appropriate for a medical purpose. Neurofolin is a food for special medical purposes for the dietary management of depression. It contains 15mg of L-methylfolate, a form of folate hat helps nutritionally support mood regulation for people suffering from depression.
Neurofolin can be taken together with your current antidepressant therapy or alone, as advised by your healthcare professional. This statement was intended to fulfil the requirements of Standard 2.9.5-10(c) and (d), indicating the medical purpose of the food, and/or describing the characteristics that make it appropriate for a medical purpose.
The statement also addresses the definition of a FSMP (ie, "intended to be used under medical supervision") and make clear how Neurofolin can be used. Neurofolin can be used together with your current antidepressant therapy as advised by your healthcare professional.
Once in the brain, it supports the production of serotonin and noradrenaline. This statement was not intended as a therapeutic claim, but was included to draw a parallel with the permitted general level health claims for folate (ie, that it contributes to normal psychological function). General level health claims are not therapeutic claims. Neurofolin contains an active form of folate to help nutritionally support normal psychological function.
Unlike some tablet formulations, Neurofolin has been specifically formulated for the dietary support of depression management and contains 15 mg of L-methylfolate. This statement was intended to fulfil the requirements of Standard 2.9.5-10(c) and (d), indicating the medical purpose of he food, and/or describing the characteristics that make it appropriate for a medical purpose. Neurofolin has been specifically formulated for the dietary management of depression and, unlike some tablets containing folate, it contains an active form of folate in a quantity to nutritionally support mood regulation for people suffering from depression.

Next Steps
We trust hat these clarifications address the TGA's concerns. We would appreciate the opportunity to speak with you further, either by phone or in person.
We remain available to work collaboratively with the TGA to resolve any outstanding concerns.
Yours sincerely,
s22 [redacted]

s22
s22 @grunbio ics.com<s22 @grunbiotics.com> /s22
Grunbiotics Pty Ltd
+s22
Level 9, 401 Collins Street, Melbourne Victoria 3000, Australia
http://www.grunbio ics.com

[attachment "ATT74531 1.jpg" deleted by s22 /HeadOffice/DHS]

"Important: This transmission is intended only for the use of the addressee and may contain confidential or legally privileged information. If you are not the intended recipient, you are notified that any use or dissemination of this communication is strictly prohibited. If you receive this transmission in error please notify the author immediately and delete all copies of this transmission."[attachment "Cover Letter TGA 211218.pdf" deleted by s22 HeadOffice/DHS] [attachment "Grunbiotics - s22 advice 211218.pdf" deleted by s22 /HeadOffice/DHS] [attachment "TGA Scientific response 211218 final.pdf" deleted by s22 HeadOffice/DHS]

"Important: This transmission is intended only for the use of the addressee and may contain confidential or legally privileged information. If you are not the intended recipient, you are notified that any use or dissemination of this communication is strictly prohibited. If you receive this transmission in error please notify the author immediately and delete all copies of this transmission."

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"Important: This transmission is intended only for the use of the addressee and may contain confidential or legally privileged information. If you are not the intended recipient, you are notified that any use or dissemination of this communication is strictly prohibited. If you receive this transmission in error please notify the author immediately and delete all copies of this transmission."

---

s47B

s47B

s47B

s47B

From: s22
To: Francis, Jenny; s22 ; MCLAY, Nicole
Cc: s22
Subject: FW: Grunbiotics Pty Ltd - Neurofolin (RIES 26886) [SEC=OFFICIAL, ACCESS=Legal-Privilege]
Date: Thursday, 18 April 2019 11:19:12 AM
Attachments: [D19-5408451] RIES26886 Grunbiotics - letter from Dept of Health and Human Services dated 11 April 2019.PDF
image003.jpg
image001.png

FYI. State regulator's view on Grunbiotics.
We're still awaiting s42 .
Regards,

s22
s22

Legal Advisings Section | **Regulatory Legal Services Branch**
Health Products Regulation Group
Australian Government Department of Health
PO Box 100 Woden ACT 2606
T: s22 | E: s22 @health.gov.au

From: s22 **On Behalf Of** s22
Sent: Thursday, 18 April 2019 11:04 AM
To: s22
Cc: s22 ; s22
Subject: Grunbiotics Pty Ltd - Neurofolin (RIES 26886) [SEC=OFFICIAL, ACCESS=Legal-Privilege]

Good morning,
Please find attached letter dated 11 April 2019 from Department of Health and Human Services, Victoria concerning 'Neurofolin' marketed and manufactured by Grunbiotics Pty Ltd.
Regards, s22

s22
s22
Regulatory Compliance Section
Regulatory Practice, Education and Compliance Branch

Phone: s22
Email: s22 @health.gov.au

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
www.tga.gov.au

Document 3

Department of Health and Human Services

50 Lonsdale Street
Melbourne Victoria 3000
Telephone: 1300 650 172
GPO Box 4057
Melbourne Victoria 3001
www.dhhs.vic.gov.au
DX 210081

HHSD/19/150090

s22 [redacted]

Regulatory Compliance Section
Regulatory, Education and Compliance Branch
Therapeutic Goods Administration
Department of Health
PO Box 100
WODEN ACT 2606

Dear s22 [redacted]

I refer to the product "Neurofolin" manufactured and marketed by Grünbiotics. I also refer to the letter from Grünbiotics to the Therapeutic Goods Administration (TGA), dated 21 December 2018 and to the materials provided by Grünbiotics in support of its claim that Neurofolin is a Food for Special Medical Purposes (FSMP).

I understand that the TGA conducted an initial assessment of Neurofolin and formed the view that Neurofolin is mostly likely a "therapeutic good" within the meaning of section 3(1) of the *Therapeutic Goods Act 1989* (Cth).

The TGA referred Grünbiotics to the Department of Health and Human Services (department) to determine, in its capacity as regulator under the Australian and New Zealand Food Standards Code (Code), whether Neurofolin is a FSMP as defined in Standard 1.1.2 and noted in Standard 2.9.5 of the Code.

On 3 December 2018, the Food Safety Unit of the department met with Grünbiotics. By letter dated 6 December 2018 (enclosed), Grünbiotics provided the department with additional medical evidence to support Grünbiotics' claim that Neurofolin is a FSMP.

On the basis of its assessment of the evidence provided and discussions with Grünbiotics, the department is of the view that Neurofolin is better classified as a therapeutic good under the operation of the *Therapeutic Goods Act 1989* (Cth) for the following reasons:

- Neurofolin is marketed to individuals with depression at large;
- it is questionable whether a person with any type of depression will have identifiable, established special medically determined nutrient requirements;
- the level of Neurofolin's key ingredient L-methylfolate calcium is extraordinarily in excess of the recommended dietary intake, which makes Grünbiotics' claim that Neurofolin is for dietary management and not therapeutic use questionable.

The department refers the matter to the TGA to take the necessary action.

I note that any determination in respect of Neurofolin is likely to have wider regulatory impacts as there are similar products on the market that are marketed as a FSMP currently (product information for these products is enclosed).

Should you require the department's further assistance with this matter, please contact s22 s22 Food Safety Unit on s22 or email s22 @dhhs.vic.gov.au.

Yours sincerely

s22

s22 Food Safety Unit
Regulation Health Protection and Emergency Management

11 / 4 / 2019

Encl.
1. Letter to s22 dated 6 December 2018.
2. Product information for Souvenaid® and Cubitan.

6 December 2018

GRÜNBIOTICS
Medical Nutrition. Improving Lives.

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ACN: 610 953 878
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s22
50 Lonsdale Street
Melbourne Victoria 3000

Dear s22 and s22

INTERPRETATION OF STANDARD 2.9.5

We refer to our meeting on Monday 3rd December 2018, where – as suggested by the Therapeutic Goods Administration – we discussed the appropriacy of classifying Neurofolin as a food for special medical purposes (**FSMP**) under Standard 2.9.5 of the *Australia New Zealand Food Standards Code* (**the Food Standards Code**).

Our key objectives in this meeting and in engaging further with the Victorian Department of Health are:

- to clarify how the legal definition of an FSMP in Standard 2.9.5 does or does not apply to Neurofolin; and
- if necessary, engage in further discussion with the Victorian Department of Health to bring Neurofolin into compliance with Standard 2.9.5.

Following our meeting, you requested the medical evidence we rely on in classifying our product as an FSMP. Please find **enclosed** with this letter a summary of the studies (both from Australia and overseas) demonstrating the causal connection between certain forms of depression and an inability to adequately metabolise folate from ordinary food/diet. These studies also clearly demonstrate why the levels of folate in Neurofolin are necessary to manage the diets of people with certain forms of depression.

An outcome of our meeting was further internal discussion with the Compliance Team at the Victorian Department of Health. We would appreciate it if this further discussion were directed towards answering the following question:

How does a product:

- *in a food format;*
- *comprised of ingredients permitted in food;*
- *that is specially formulated for the dietary management of individuals whose capacity is impaired to metabolise certain nutrients in ordinary food;*
- *whose dietary management cannot be completely achieved without the use of the food; and*
- *is intended to be used under medical supervision*

***not** meet the definition of a food for special medical purposes?*

In order to assist with this internal discussion, we now summarise the issues raised in our meeting:

1. Dietary management of individuals with special medically determined nutrient requirements may be – depending on the medically determined need – highly specific and limited to a small number of "certain nutrients".
2. Standard 2.9.5 deliberately does not set any maximum limits for nutrients and nutritive substances permitted by the Food Standards Code so as to allow manufacturers to supply products designed to meet the special medically determined nutrient requirements of the individuals in question.
3. Standard 2.9.5 expressly **includes** products which only provide partial feeding. As a result, there are many FSMP products on the Australian market that have been designed to meet special medically determined nutrient requirements, and as such do not necessarily include any macronutrients nor provide whole of diet solutions.
4. Neurofolin has been designed to meet the regulatory definition of an FSMP. Scientific, medical and regulatory experts were extensively consulted ahead of launching the product in Australia to ensure it met the definition of a FSMP. While it does contain high quantities of folate (among other ingredients), the evidence demonstrates that this is the level required to address the special medically determined nutrient requirements of individuals suffering from certain forms of depression.

5. It would **not** be appropriate to classify the product as a therapeutic good or as a vitamin supplement because:
   - Therapeutic equivalents to Neurofolin would **not** adequately manage the diets of people suffering from certain forms of depression – only the FSMP pathway allows for the product to be designed in the required way; and
   - The product does **not** treat depression. It addresses a dietary imbalance created by certain forms of depression which – under medical supervision – can lead to better health outcomes using therapeutic products designed to actually treat depression.
6. We understand that statements of medical purpose can risk being interpreted as a prohibited therapeutic claim or a prohibited claim for therapeutic use. We would welcome the opportunity to work with the Department of Health to ensure that any claims are compliant with Standard 2.9.5.
7. As stated by Erica in our meeting, the intent behind the creation of Standard 2.9.5 was to allow Australian consumers access to products aimed at their special medically determined nutrient requirements, most of which were originating from Europe. We note that Neurofolin is registered in the EU as an FSMP.
8. Should products like Neurofolin be determined to not be foods for special medical purposes, there would be a large number of products currently available on the market in Australia and being developed in Europe that would not be permitted to reach Australian consumers with special medically determined nutrient requirements.
9. Neurofolin is currently being used by over 2000 Australian consumers (and growing) to manage the dietary imbalances caused by their depression, which in turn allows them to achieve better health outcomes under medical supervision.

Kind Regards,

s22

Neurofolin® is specifically formulated for the dietary management (as opposed to treatment) of individuals.

1) **The scientific literature supports a medically determined nutrient requirement.**

- Numerous studies looking at populations of individuals diagnosed with depression have observed a significant deficit in folate levels in red blood cell and serum levels [1–5].
- Approximately 30.4% to 64% of patients suffering from Major depressive disorder (MDD) display a red blood cell folate deficiency, with about 36% of MDD patients showing cerebral 5-MTHF deficiency (where serum folate levels are normal but cerebral spinal fluid 5-MTHF is low) [6–8].
- This relationship has been confirmed through multiple robust meta-analyses (the most reliable form of evidence) which have concluded a significant relationship between folate status and depression, even after adjusting for potential confounds [13,14].

As such, given the preponderance of evidence, patients diagnosed with depression have a medically determined nutrient requirement.

2) **It is not sufficient to simply provide these individuals with regular dietary folate or other forms of vitamins that would not be equivalent to requiring FSMP status.**

- Evidence shows that up to 70% of MDD patients are carriers of the MTHFR C677T allele, showing either a C677T heterogeneous or homogenous polymorphism [7,15–19].
- These patients show a markedly reduced ability to convert folate to L-5-Methylfolate (L-5-MTHF), a feature not able to be remedied by intake of normal food. Therefore, this relatively common mutation can lead to a functional alteration of the metabolic processing of folate to L-5-MTHF, resulting in a deficiency of L-5-MTHF in the cerebrospinal fluid (CSF).
    - This specific polymorphism therefore results in an inborn error of metabolism and has been found to be associated with depression in numerous studies [15,18,20–23].
- Finally, this association has been confirmed across multiple meta-analyses, supporting a significant association with the MTHFR C677T polymorphism and a clinical diagnosis of MDD [23–25].
- Among numerous metabolic functions, 5-MTHF is important for the conversion of homocysteine to methionine.
    - This step is performed by the vitamin B12-dependent methionine synthase.
    - To achieve appropriate conditions for the normal metabolic functions, the levels of 5-MTHF and Vitamin B12 must both be in the optimal range.

Therefore, it may be seen that dietary management is required for individuals diagnosed with MDD.

3) **The specific formulation of Neurofolin® has been determined to address this inborn error of metabolism, addressing the dietary requirement, based on scientific evidence with two key vitamins of note: L-5-MTHF (the bioavailable version of folate, to bypass the established MTHFR C677T polymorphism) and vitamin B12.**

- Numerous clinical studies in humans have found that 15mg/day of L-5-MTHF, was effective in addressing the underlying dietary deficiency in outpatients with SSRI-resistant MDD [16,17,26–28].
- This dietary management only resulted in significant improvements when combined with standard SSRI treatment, when compared with outcomes relative to SSRI treatment alone.
    - It can be seen that dietary management was never intended for therapeutic use.
- In these trials, the dose of 7.5mg/day did not show a significant improvement [16,17,26–28].
- As such, it must be considered that providing patients with MDD less than 15 mg/day of L-5-MTHF is insufficient to meet the dietary deficiency that allows the pharmacological treatment of MDD to work effectively.
- **High dose Folic Acid supplementation (the unmethylated synthetic form) has been shown to be inadequate for those patients and has potentially dangerous side-effects as it is unlikely to be processed in many of these patients [7,29] . L-5-MTHF is a soluble, as such any intake which is excess to requirements is excreted through urine.**
- Evidence supporting the value of including vitamin B12 come from multiple studies. Several studies identified the relation between depression and low serum Vitamin B12 levels [30–32].
- Subjects with vitamin B12 deficiency were 70% more likely to have severe depressive disorder than subjects without deficiency [30,31]. As for higher folate status, higher vitamin B12 status was associated with better treatment outcome when treated with antidepressants ([33,34]; for review see also[35]).
- Therefore, an optimal vitamin B12 supply is especially important for MDD patients. Neurofolin® contains in addition to the 15mg of L-5-Methyltetrahydrofolate calcium, 1mg Cyanocobalamin (vitamin B12), from which approximately 1% gets absorbed[58].

- This dosage is generally considered as being adequate for an optimal vitamin B12 supply for MDD patients (review see [52]). Please note, again this is only relevant for the supply of required vitamins and does not relate to any therapeutic use.
- In addition, the formulation of the product is a sachet to be dissolved in water. MDD patients, being on SSRI medication (conventional therapy for MDD) often suffer from symptoms of dry mouth. The specific formulation has taken this into account and will help to increase the compliance.

From this it may be seen that the product Neurofolin® is specifically formulated to address a dietary imbalance associated with a group of individuals. Neurofolin® is neither intended nor advertised as having a therapeutic effect. Moreover, there is not a single peer reviewed study which has found that any of the ingredients in Neurofolin, nor the combination of ingredients may exert a therapeutic effect alone.

4) **Neurofolin® should not be taken for a therapeutic effect as no evidence supports this use.**

- Dietary management with L-5-MTHF alone, without pharmaceutical treatment is not sufficient for patients suffering from MDD [16,17,26–28].
    - As such, Neurofolin® is not suitable as a monotherapy or for therapeutic use alone.
- Dr Josephine Anderson, Clinical Director of the Black Dog Institute when asked about L-methylfolate stated "There is certainly no robust evidence for their effectiveness as a treatment by themselves". (www.9news.com.au Sept 16 2017).
- No study has tested dietary management with L-5-MTHF as a monotherapy, nor does any study recommend that it should be considered for therapeutic use [16,17,26–28].
- No claims will be made to suggest that Neurofolin® is likely to exert a therapeutic function beyond addressing a dietary imbalance commonly associated with depression. Any existing claims which may be interpreted in such a way will be modified to ensure accuracy.

The scientific information summarized above, shows, that Neurofolin® is **not designed to treat, cure or alleviate any disease state, but is specially formulated for the adjunctive dietary management of patients suffering from depression to fulfil their metabolic need of key vitamins.** Grunbiotics will remove any claims identified which suggest a therapeutic effect of Neurofolin®.

5) **Folate is an essential nutrient that cannot be synthesized *de novo* and must be obtained from the diet.**

- Folate must be derived from diet or supplementation. Dietary folate in the form of dihydrofolate is found in leafy green vegetables, legumes, beans, liver, citrus fruits, and yeast.
- Moreover, due to widespread genetic inability of many of these individuals to process dietary folate, providing excess dietary folate would be largely inefficient to address the dietary imbalance.
- The bioactive 5-MTHF, which is the relevant form for the target patient group, is present in ordinary food in very limited amounts, with cauliflower being one of the richest sources (up to 100µg/100g) [36,37]. These levels are only exceeded by germinated legume seeds (such as mung bean), which show peak values of L-methylfolate 4 days after germination up to 450µg/100g [38].

These numbers show, that consumption of normal food does not allow depressed patients to achieve a daily dose of 15mg L-methylfolate, as a regular daily consumption of e.g. 3kg mung bean sprouts would be required to achieve a comparable supply of the vitamin 5-MTHF per day.

6) **The required quantity of vitamins observed to be required to achieve dietary management exceeds that reasonably obtainable otherwise.**

- As discussed above the amount of 15mg/day of L-5-MTHF included in Neurofolin® is based on clinical trials where this dosage was required to meet the dietary deficiency of the target patient group of those with MDD which in turn allowed for the pharmacological treatment to be more effective.
- Therefore, the higher dose is not a therapeutic dose it is a nutritional dose designed to nutritionally address the medically established dietary deficiency to allow SSRI treatment to function as intended.
- The higher dose may be required for three key reasons;
    - I. Folic acid from food sources taken in the course of daily life still undergoes processing, even in those who cannot convert it to L-5-MTHF. As such the absorption of Neurofolin® may be limited as metabolites are preoccupied with forms that are unable to be processed efficiently [39].
    - II. It is noted that higher dietary requirements may be required for those diagnosed with depression than for the general population [9–12].
    - III. If individuals have a chronic deficiency the higher dose is needed to address this metabolic imbalance more swiftly. Given that patients with depression are widely known to have impaired appetitive motivation, it is important that any food aimed to assist with the dietary management contains suitably

high concentrations to deal with this aspect.

- Finally, consumption of dietary supplements is not suitable to cover the requirement of 5-MTHF. To our knowledge, there is only one supplement on the Australian market, *BioCeuticals MTHF*, delivering a dose of 500mcg per day.
    - This would unreasonably require the consumption of 30 tablets/day to achieve the required dose of 15mg 5-MTHF per day and lacks B12. As such it is not a suitable replacement.

In conclusion, the dose of 15mg/day of L-5-MTHF required for effective dietary management of individuals diagnosed with MDD **exceeds amounts that may be reasonably obtained from conventional food sources or other products that are not FSMPs**.

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Souvenaid®

A food for special medical purposes that nutritionally supports memory function during the early stages of Alzheimer's disease[1,2]

Features

- Souvenaid is a food for special medical purposes that nutritionally supports memory function during the early stages of Alzheimer's disease
- Souvenaid contains a unique combination of nutrients, called Fortasyn™ Connect, designed to meet the specific nutritional needs of people in the early stages of Alzheimer's disease. These include: **Omega 3 Fatty Acids (DHA* EPA*), UMP#, choline, B vitamins, selenium, phospholipids**
- Available in three flavours: vanilla, strawberry and cappuccino
- Gluten and lactose free
- Low Glycaemic Index of 50 for Strawberry and Vanilla flavours only

Ingredients^

Souvenaid Vanilla: Water, maltodextrin, sugar, fish oil, milk proteins, flavouring (vanilla), uridine 5'-monophosphate disodium salt, choline chloride, acidity regulator (citric acid), stabilisers (microcrystalline cellulose and sodium carboxymethylcellulose), potassium citrate, soy lecithin, calcium hydroxide, sodium L-ascorbate, DL-α tocopheryl acetate, magnesium hydroxide, potassium hydroxide, sodium chloride, sodium selenite, ferrous lactate, sodium citrate, colour (curcumin), pteroylmonoglutamic acid, cyanocobalamin, zinc sulphate, retinyl acetate, nicotinamide, pyridoxine hydrochloride, copper gluconate, manganese sulphate, chromium chloride, calcium D-pantothenate, D-biotin, cholecalciferol, thiamin hydrochloride, sodium molybdate, riboflavin, potassium iodide, phytomenadione

^Please note the ingredients list is for Vanilla flavour only. There are minor variations in the ingredients list between different flavours. For the full ingredients list, please contact the Nutricia Clinical Care Line on 1800 060 051.

Ordering Information

- Order online www.nutriciastore.com.au
- Phone Nutricia Customer Service 1800 884 367
- Buy in-store from pharmacy

Souvenaid	Code	Units per carton
Vanilla	127781	24 x 125ml
Strawberry	127789	24 x 125ml
Cappuccino	127802	24 x 125 ml

Souvenaid Connections

Souvenaid Connections is an exclusive support programme for patients with early Alzheimer's disease who have been recommended to take Souvenaid.
To become a member, please register at www.souvenaid.com.au For further information please call **1800 884 367.**

Indications

- For the dietary management of early Alzheimer's disease
- To be used as a supplement to the normal dietary intake (not suitable as sole source of nutrition).

Contraindications

- Not for intravenous use
- Not suitable for patients with allergies to fish oil, milk or soy
- Not suitable for patients with Galactosaemia

Precautions

- Souvenaid does contain carbohydrate and as with other foods containing carbohydrate, it is advisable for people with diabetes to monitor their blood glucose levels as per normal.

Directions for use

- Souvenaid is designed to be taken as one bottle (125ml) once a day, in addition to the normal dietary intake
- The length of use of Souvenaid by an individual should be determined by their healthcare professional
- Shake well before use
- Ready to drink and best served chilled

Storage

- Store in a cool, dry place
- Once opened, store in the refrigerator
- Discard unused contents after 24 hours

References: 1. Scheltens P, et al. Alzheimers Dement. 2010 Jan;6(1):1-10. 2. Scheltens P, et al. J Alzheimer's Dis. 2012;31:225-236

A Food for Special Medical Purposes; intended to be used under medical supervision.

For more information call the Nutricia Clinical Care Line **1800 060 051**

NC3421-Mar17

NUTRICIA Advanced Medical Nutrition

Souvenaid®

Nutrition Information		Per 100ml	Per 125ml bottle
Energy	kcal	100	125
	kJ	420	525
Protein	g	3 (12%)	3.75
Carbohydrate	g	13.2 (52%)	16.5
Sugars	g	6.4	8
as Lactose	g	Nil detected	Nil deteced
as Fructose	g	0	0
Fat	g	3.9 (36%)	4.9
Saturates	g	1.2	1.6
Monounsaturates	g	0.7	0.9
Polyunsaturates	g	1.5	1.9
EPA*	mg	240 (238)	300 (298)
DHA*	mg	960 (951)	1200 (1189)
ω6 / ω3 ratio		0.18:1	0.18:1
Fibre	g	0 (0%E)	0
Water	g	84	105

Minerals			
Sodium	mg	100	125
	mmol	4.3	5.4
Potassium	mg	150	188
	Mmol	3.8	4.8
Calcium	mg	80	100
Phosphorus	mg	70	88
Magnesium	mg	20	25
Chloride	mg	125	156
Ca:P ratio		1.1:1	

Other			
Uridine 5'-monophosphate#	mg	500	625
Choline	mg	320	400
Osmolarity	m0smol/l	465 490 495	

*DHA: docosahexaenoic acid, EPA: eicosapentaenoic acid (DHA & EPA are omega-3 polyunsaturated fatty acids)
#UMP: uridine monophosphate

Vitamins		Per 100ml	Per 125ml bottle
Vitamin A	µg-RE	160	200
Vitamin D	µg	0.7	0.9
Vitamin E	mg-α-T.E.	32	40
Vitamin K	µg	5.3	6.6
Vitamin C	mg	64	80
Thiamin	mg	0.15	0.2
Riboflavin	mg	0.16	0.2
Niacin	mgNE	1.8	2.3
Vitamin B6	mg	0.8	1
Vitamin B12	µg	2.4	3
Folic Acid	µg	320	400
Pantothenic Acid	mg	0.53	0.7
Biotin	µg	4	5

Trace Elements			
Iron	mg	1.6	2
Zinc	mg	1.2	1.5
Manganese	mg	0.33	0.4
Copper	µg	180	225
Iodine	µg	13	16.2
Molybdenum	µg	10	12.5
Selenium	µg	48	60
Chromium	µg	6.7	8.4
Fluoride	mg	0	0

Nutritional Needs in early Alzheimer's disease

This is the amount of food you need to consume on top of your daily intake to achieve the same level of key nutrients in one bottle of Souvenaid.

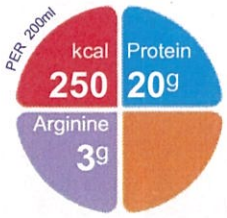
Trace Elements	Souvenaid Amount	Dietary Equivalent
DHA	1200mg	4 tins tuna/100g Fresh Tuna
EPA	300mg	4 tins tuna/100g Fresh Tuna
UMP	625mg	1kg tomatoes
Choline	400mg	100g minced beef
Phopholipids	106mg	4 eggs
Folic Acid	400µg	1.2kg broccoli
Vitamin B6	1mg	710g Spinach
Vitamin B12	3µg	Contained in tuna
Vitamin C	80mg	1 orange
Vitamin E	40mg	Contained in tuna portion
Selenium	60µg	Handful of brazil nuts

Cubitan

A ready-to-drink, nutritionally complete oral supplement enriched with nutrients essential for wound healing including arginine, vitamin C and zinc. Contains 250kcal, 20g protein and 3g arginine per 200ml bottle.

Features

- High protein to facilitate wound healing[1]
- Arginine enriched, 3g per bottle, to enhance collagen deposition for wound healing[2,3]
- Enriched with vitamin C, 250mg per bottle, with antioxidant properties and to aid collagen synthesis[3]
- Zinc enriched, 9mg per bottle, to enhance tissue regeneration[3]
- Vitamin E enriched, 38mg per bottle, for its antioxidant properties[3]
- Addition of carotenoids and flavenoids to regulate inflammatory processes
- User friendly, easy to hold plastic bottle with straw attached and resealable cap



Storage

- Store in a cool, dry place
- Once opened, store in the refrigerator
- Discard unused content after 24 hours

Ordering Information

- To order contact Nutricia Customer Care 1800 889 480

Cubitan	Presentation	Code	Units per carton
Vanilla	200ml bottle	41267	24

Indications

For the dietary management of:

- Pressure ulcers
- Chronic wounds

Important Notice

- Not suitable for patients with galactosaemia
- Not suitable for infants under 1 year of age
- Use with caution in children aged 1-6 years

Directions for Use

- Shake well before use
- Best served chilled
- Usage to be determined by a healthcare professional
- **Suggested intake:**

Pressure Ulcer Stage	Cubitan (bottles/day)
1 (subcutaneous wound)	1
2 or 3 (superficial wound)	2
4 (deep wound)	3

Ingredients

Cubitan Vanilla: Milk protein, water, maltodextrin, sugar, vegetable oils (rapeseed oil, sunflower oil), L-arginine, acidity regulator (citric acid), flavour (vanilla), sodium L-ascorbate, carotenoids (contain **soy**), (β-carotene, lutein, lycopene), magnesium hydrogen phosphate, emulsifier (**soy** lecithin), choline chloride, di potassium hydrogen phosphate, DL-α-tocopherol, potassium citrate, magnesium hydroxide, ferrous lactate, potassium chloride, zinc sulphate, potassium hydroxide, sodium selenite, copper gluconate, manganese sulphate, sodium chloride, nicotinamide, retinyl acetate, pteroylmonoglutamic acid, calcium D-pantothenate, pyridoxine hydrochloride, chromium chloride, riboflavin, D-biotin, cholecalciferol, thiamin hydrochloride, sodium molybdate, sodium flouride, potassium iodide, phytomenadione, cyanocobalamin.

1. Van Anholt RD et al. Nutrition 2010; 26: 867-872
2. Stechmiller JK et al. Nutr Clin Pract 2005; 20(1): 52-61
3. Kavalkas SL & Barbul A. Plast Reconstr Surg 2011; 127(Suppl1): 385-435

A food for special medical purposes; to be used under strict medical supervision.

For more information call the Nutricia Clinical Care Line **1800 060 051**

NUTRICIA Advanced Medical Nutrition

NC3238- Aug 16

Cubitan

Nutrition Information		Per 100ml	Per serve*
Energy	kcal	128	256
	kJ	540	1080
Protein	g	10 (31%E)	20
Casein	g	6.2	12.4
Whey	g	1.5	3.0
Arginine	g	1.5	3.0
Carbohydrate	g	14.2 (44%E)	28.4
Sugars	g	7.1	14.2
as Lactose	g	1.7	3.4
Fat	g	3.5 (25%E)	7.0
Saturates	g	0.4	0.8
Monounsaturates	g	2.1	4.2
Polyunsaturates	g	1	2
ω6 / ω3 ratio		5:1	5:1
Fibre	g	0	0
Water	ml	80	160

Minerals		Per 100ml	Per serve*
Sodium	mg	50	100
	mmol	2.2	4.4
Potassium	mg	150	300
	mmol	3.8	7.6
Calcium	mg	225	450
Phosphorus	mg	182	364
Magnesium	mg	42	84
Chloride	mg	80	160
Ca:P ratio		1.2:1	1.2:1

*Serve size: 200ml

Vitamins		Per 100ml	Per serve*
Vitamin A	µg-RE	119	238
Vitamin D	µg	1.3	2.6
Vitamin E	mg-α-TE	19	38
Vitamin K	µg	10	20
Vitamin C	mg	125	250
Thiamin	mg	0.28	0.56
Riboflavin	mg	0.63	1.26
Niacin	mg NE	3.4	6.8
Vitamin B6	mg	0.65	1.30
Vitamin B12	µg	0.79	1.58
Folic Acid	µg	100	200
Pantothenic Acid	mg	1	2
Biotin	µg	7.5	15

Trace Elements		Per 100ml	Per serve*
Iron	mg	3	6
Zinc	mg	4.5	9.0
Manganese	mg	1.3	2.6
Copper	µg	675	1350
Iodine	µg	25	50
Molybdenum	µg	19	38
Selenium	µg	32	64
Chromium	µg	13	26
Fluoride	mg	0.19	0.38

Other		Per 100ml	Per serve*
Carotenoids	mg	0.75	1.50
Choline	mg	69	138
Osmolality	mOsmol/kg H_2O	625	625