From: Salvatore DAngelo
To: Deng, Kaiping
Cc: Ian Horner_Kerry; Scott Barnum_Kerry; Ryan Simon Intertek
Subject: [EXTERNAL] FW: FDA Response
Date: Wednesday, August 16, 2023 12:02:06 PM
Attachments: C85DF2FC52BD4EC99D287875EFDA32C0.png
279F24FCE94A412B942F96EAE904CF49.png

Dear Dr. Deng,

We have prepared a response to your questions regarding Calcium Acetate and offer the following. We trust this information is sufficient for approval of our application. As always lease advise if there are any questions or additional information needed.

Best Regards,

Sal D'Angelo

Sal:

I have filled in the missing data from the last email. You can share this with FDA.

Ryan

Based on feedback from customers we anticipate that calcium acetate will be used at a maximum level of 0.5% as an antimicrobial agent in most food categories, which compares to a use typical maximum use level of 0.3% for calcium propionate. In this regard it is expected that the use of calcium acetate as an antimicrobial will be partially substitutional to current uses of calcium propionate and in these instances will result in some foods containing higher concentrations of calcium. Niacet recognizes that the current dietary intakes of calcium estimated using the NHANES surveys approaches the Institute of Medicine's upper limit for calcium of 2000 mg among individuals >50 years of age. The majority of calcium consumed in the diet is contributed by natural sources (e.g., cheese, milk, vegetables) and dietary supplements, therefore changes from added sources with technical functionality in food will have a fractional impact on total dietary intakes. Among heavy consumers (90^{th} percentile), the estimated impact of added sources of calcium in the in the diet will be overestimated as such products will not have 100% marketshare, and consumers are highly unlikely to consume every food product to which calcium acetate may be added at the highest permissible use level on a daily basis. These limitations in the use of NHANES data are widely acknowledged. For example, the National Cancer Institute (NCI) have developed a method to model particular aspects of usual dietary intakes of episodically foods using 24-hour recalls (1). This method has been validated in a series of peer-reviewed publications (1) and has been applied to dietary calcium intakes using NHANES data. For example, using this method, the estimated distributions of calcium for men aged 40–59 were determined using data provide by the National Health and Nutrition Examination Survey (2011–2014). When calcium intakes were estimated using the traditional approach (i.e., NHANES) to estimate the 90^{th} percentile intakes of calcium on a given day by men aged 49 to 59, dietary intakes of calcium were estimated to be 1966**.**8 mg. This value is comparable to the 90^{th} percentile intake of 1980 mg that was estimated for calcium among men aged 31 to 50 presented in Table 3.3.1-1 in Niacet's notice. However, when dietary intakes of calcium were estimated using the NCI method which corrected for episodic consumption patterns by heavy users of foods that may contain calcium, the intakes of calcium from all food sources was estimated to be much lower at 1598.1 mg per day (2). Thus, a significant margin relative to the upper limit of 2000 mg per day is apparent and the replacement of antimicrobial food uses of calcium proprionate in the diet with calcium acetate is not expected to result in dietary intakes that would exceed the UL value of 2000 mg among older individuals <50

years of age.

1. Usual Dietary Intakes: The NCI Method | EGRP/DCCPS/NCI/NIH (cancer.gov)
2. Vital and Health Statistics, Series 2, Number 178, February 2018 (cdc.gov)

Ryan Simon
Sr. Director, Safety & Regulatory
Food & Nutrition Group

Direct +1 905 286-4188
Office +1 905 542-2900
http://www.intertek.com/scientific-regulatory-consultancy/

Intertek, 2233 Argentia Rd., Suite 201, Mississauga, ON L5N 2X7

Niacet
400 47th Street
Niagara Falls, NY 14304
USA
T + 1 716 285 1474
www.niacet.com

December 4 ,2023

Kaiping Deng, Ph.D.
Division of Food Ingredients
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD
20740-3835 USA

Re: GRAS Notice No. GRN 001126

Dear Dr. Deng,

Please see the below responses to the United States (U.S.) Food and Drug Administration (FDA)'s letter dated November 2nd, 2023 pertaining to information provided within Niacet's Generally Recognized as Safe (GRAS) Notice for calcium acetate filed by the Agency under GRN 001126.

FDA.1. *On page 5, Niacet states that the starting materials for the production of calcium acetate are calcium hydroxide and acetic acid. However, in Table 2.5-1, the starting materials are indicated to be calcium oxide, water and acetic acid. Please clarify this discrepancy.*

Calcium oxide is the correct starting material.

FDA.2. *Please clarify what the footnotes in Figure 2.5-1 represent, i.e., please provide footnotes for the superscripts 1, 2 and 3 in the flowchart.*

Footnotes are included in the lower box. (CCP1, 2, & 3). Critical Control Points

FDA.3. *Please provide details on the methods used to establish the specifications for calcium acetate including method designation for compendial methods or in-house developed methodology. Please confirm that the analytical methods used for establishing the specifications have been validated for their intended purposes.*

All specifications including compendial methods meet the requirements of FCC 1

1Attached is the results batch analyses for lot BL-2021-5226 demonstrating that lead is below a detection limit of 0.125 mg/kg and arsenic is below a detection limit of 0.375 mg/kg.

Niacet
400 47th Street
Niagara Falls, NY 14304
USA

FDA.5. *Please indicate why there is one order of magnitude difference between the batch analysis for fluoride in Table 2.7-1. Please provide actual data with the corresponding limits of quantification for the methods.*

The certificate of analysis for this lot reports the data for fluoride as compliant with the specification rather than reporting a quantitative value. We will provide additional lots of material demonstrating compliance with the specification once recent testing is completed.

FDA.6. *Please specify the method for the determination of mercury in calcium acetate.*

Mercury is not listed as an FCC requirement; however, Mercury is tested by the FCC mercury limit test.

FDA.7. *Please confirm that the specifications for calcium acetate conform to the most recent edition of the Food Chemicals Codex, i.e., FCC 13.*

Yes, the specifications for calcium acetate conform to the most recent edition of the FCC.

FDA.8. *Please confirm that the intended uses of calcium acetate will be substitutional to calcium lactate and calcium propionate up to a maximum use level of 0.5%.*

Yes, Niacet confirms that the intended use of calcium acetate will be substitutional to calcium lactate and calcium propionate up to a maximum use level of 0.5%.

FDA.9. *In the amendment from August 16, 2023, Niacet proposes to use the NCI method of usual intakes for estimation of calcium dietary exposure. Please provide a dietary exposure estimate for the cumulative exposure to calcium using the NCI usual intake method.*

The NCI usual intake method requires complicated statistical analyses and Niacet is not able to provide such information; however, as the intended uses of calcium acetate are substitutional to the current GRAS uses of calcium propionate under 21 CFR § 184.1221 and calcium lactate under 21 CFR § 184.1207 no increase in dietary intakes of calcium are expected.

FDA.10. *On page 4, Niacet states that "Calcium acetate is used in the following foods as an antimicrobial agent at levels not to exceed current good manufacturing practices (cGMP): baked goods; cheeses; confections and frostings; gelatins, puddings, and fillings; and jams and jellies. These food uses are fully substitutional to the current GRAS uses of calcium propionate under 21 CFR § 184.1221 (U.S. FDA, 2021)."*

In the Appendix A of the GRAS notice, Niacet and AIB International evaluated the antimicrobial activities of three compounds: calcium acetate, calcium propionate-granular and calcium propionate-crystal in baked bread in 2003. The use levels were 0.1875% and 0.3125% flour basis. According to the data in Table III- Mold Results on page 8 of Appendix A, calcium acetate was not as effective as calcium propionate at both levels. On page 4 of Appendix A, Niacet and AIB International also concluds that "The bread containing- 0.3125% Calcium Propionate - Crystal had the longest storage time before all of the test samples showed evidence of mold growth." The result of the study does not support the following statements in Part 2.8 (page 9) of the GRAS notice "Effective antimicrobial activity against various spoilage organisms and microbial pathogens also have been demonstrated experimentally with highly comparable antimicrobial activity observed between calcium acetate and calcium propionate. These studies demonstrate that in the U.S., calcium acetate would be suitable for use in foods as a substitute for calcium propionate."
Please provide additional data to support the proposed antimicrobial functionality that calcium acetate will be used substitutionally to calcium propionate at the level of 0.2 to 0.5% in the proposed food categories.

Niacet does not have further studies comparing the antimicrobial properties of calcium acetate and calcium propionate. These types of studies are typically conducted by the food manufacturer to determine the most effective concentration of each substance under the use limitations of up to 0.5%. Niacet recognizes that in some food applications higher concentrations of calcium acetate relative to calcium propionate may be necessary to achieve an equivalent antimicrobial effect; however, as the contribution of calcium acetate a calcium propionate to the total intake of calcium in the diet from antimicrobial uses of these substances is trivial relative to background consumption estimates which include uses in dietary supplement. The relative difference in efficacy of calcium acetate to calcium propionate are not relevant to the safety evaluation.

FDA.11. *On Part 6.1 (page 19), Niacet states that "The safety of calcium acetate as a multipurpose food ingredient for various specified food uses and use levels (i.e., as a firming agent, pH control agent, processing aid, sequestrant, stabilizer and thickener, texturizing agent, flavor enhancer) has been previously evaluated by the U.S. FDA and was affirmed as GRAS under 21 CFR § 184.1185 and 21 CFR § 182.6197 (U.S. FDA, 2021)." We note that the use of flavor enhancer is not listed under 21 CFR § 184.1185 and 21 CFR § 182.6197. Please clarify the regulatory information for using calcium acetate as a flavor enhancer*

The agency is correct. Use of calcium acetate as a flavoring agent under 21 CFR 184.1185 was incorrect. The correct regulatory citation for use of calcium acetate in food as a flavoring agent is FEMA GRAS No. 2228.

FDA.12. *In Part 2.8 (page 9), Niacet states that "Typical recommended use levels of calcium acetate for antimicrobial food uses on products such as bread and cut produce range between 0.2 to 0.5%". Niacet cites a webpage in footnote 2: https://www.niacet.com/product/calcium-acetate-food/. The link is re-directed to https://www.kerry.com/products/functional-ingredients/food-protection-and-preservation when it is clicked. Under "Conventional Preservation in Bakery" on the webpage, it shows that "Progusta: Food-grade acidifiers based on single (di)acetate salts". Please clarify whether this is the correct website, and where the typical recommended use levels of calcium acetate are described.*

Yes, this is the correct website; however, it does not list the recommended use levels of calcium acetate.

FDA.13. *Please provide updated information on the literature search(es) performed to prepare the notice. This includes the date(s) (e.g., month and year) of the search(es), the resource database(s) used (e.g., PubMed), the principal search terms used, and the time period that the search spanned (e.g., 1/2000 to 10/2023).*

Niacet conducted comprehensive literature searches, which were described in detail in GRN 1126 on pages 19 and 20. data and information relevant to the safety of calcium acetate using the following literature search strategy:

- **Update of the literature search conducted for calcium in GRN 6345:** GRN 634 included studies relevant to the safety of calcium that were identified via literature searches on PubMed in October 2013 and updated in June 2014, October 2015, and February 2016. A literature search strategy similar to the strategy used by PepsiCo, Inc. was used to identify new studies published since 2016.
- **Literature search on calcium acetate:** A literature search was conducted on PubMed, without date restriction, to identify studies relevant to the safety of calcium acetate.
- **Literature search for meta-analyses and/or systematic reviews on calcium:** Given that there are many human studies on the health benefits of calcium, a literature search for meta-analyses or systematic reviews of these human studies was conducted. Meta-analyses or systematic reviews published since 2016 were searched for on PubMed.
- **Literature search for meta-analyses and/or systematic reviews on acetate:** A literature search was conducted on PubMed, without date restriction, to identify meta-analyses or systematic reviews of human studies on acetate (or "acetic acid" or "vinegar").

Niacet does not agree that repeating these timely systematic searches will provide useful information to support a GRAS conclusion. Niacet has conducted supplementary manual searches of the PubMed and the internet on the safety of calcium and is not aware of any recently published evidence that is of sufficient merit to call into question the current upper limit for dietary calcium established by the Food and Nutrition Board of the Institute of Medicine. Given the ubiquitous use of calcium in the diet, it is Niacets view that if such information was published, it would be readily apparent in-line with general availability and general consensus standards of the GRAS procedure. If the agency is aware of published information that calls into question the current Upper Limits established by the IOM, Niacet would greatly appreciate such data and information from the agency in this regard.

Sincerely,

[redacted]

Salvatore J. D'Angelo
Consultant, Quality Assurance & Regulatory Affairs

Niacet Corporation A Kerry Company
400 47th Street
Niagara Falls, NY 14304

From: Salvatore DAngelo
To: Deng, Kaiping
Cc: Ian Horner_Kerry; Ryan Simon Intertek; Pieter Paul Lamers; Pieter Timmermans
Subject: FW: [EXTERNAL] RE: Questions to Notifier_GRN 001126
Date: Friday, December 22, 2023 11:04:44 AM
Attachments: 35C8B55E0B1A467BAFA8939284435D7A.png
CoA 2000096166 Calcium Acetate powder pharma .pdf
CoA 2000105017 Calcium Acetate powder pharma .pdf
CoA 2000113251 Calcium Acetate powder pharma.pdf
CoA 20001000794 Calcium Acetate powder pharma.pdf
Kerry CoA 0007643963 Calcium Acetate agglo phama batch .pdf
CoA 2000104130 Calcium Acetate Powder Pharma.pdf

Dear Kaiping,

We are providing some certificates of analysis that include actual fluoride test results for our calcium acetate product. Please note these test results are supplied to customers which may require fluoride limitations for the pharmaceutical grade which are lower than the FCC requirements. The pharma grade Niacet calcium acetate product is manufactured in the exact same manner as our FCC grade product which requires a < 50 ppm limitation as listed in the GRAS notice.

Best Regards,

Sal D'Angelo

Sent from Mail for Windows

From: Pieter Timmermans
Sent: Friday, December 22, 2023 9:44 AM
To: Salvatore DAngelo
Cc: Katarzyna Sczudlo; Henk Jan Van Lent_Kerry; Ian Horner_Kerry
Subject: RE: [EXTERNAL] RE: Questions to Notifier_GRN 001126

Hi Sal,

PFA several CoAs from some recent batches Calcium Acetate pharma in which you will find the fluoride results.

Have a good Christmas.

BR,

Pieter Timmermans
Senior Technician
Niacet, A Kerry Company
P.O. Box 60 | 4000 AB Tiel | The Netherlands
T +31 344639262 | **E** pieter.timmermans@kerry.com
kerry.com | linkedIn: @kerry | twitter: @wearekerry

Niacet
A KERRY COMPANY

Classified as General Business

From: Salvatore DAngelo <SDAngelo@niacet.com>
Sent: donderdag 14 december 2023 16:15
To: Pieter Timmermans <pieter.timmermans@kerry.com>
Cc: Katarzyna Sczudlo <katarzyna.sczudlo@kerry.com>; Henk Jan Van Lent <henkjan.vanlent@kerry.com>; Ian Horner <ian.horner2@kerry.com>
Subject: RE: [EXTERNAL] RE: Questions to Notifier_GRN 001126

Hi Pieter,

The FDA is requesting actual fluoride test results for several recent lots of Calcium Acetate. Would it be possible you could provide this information.

Best Regards,

Sal D'Angelo

This Message Is From an External Sender
This message came from outside your organization, be CAUTIOUS, particularly with links and attachments.

Dear Mr. D'Angelo,

During our review of GRAS Notice No. 001126, we noted some questions to be addressed. Please see the attached letter. Thank you and let me know if you have any questions.

Best regards,
Kaiping

Kaiping Deng, Ph.D.
Regulatory Review Scientist

Regulatory Review Branch
Division of Food Ingredients
Office of Food Additive Safety
FDA/CFSAN
Tel: 708-924-0622
kaiping.deng@fda.hhs.gov

Description
CALCIUM ACETATE PO PH 50KG

Code	**Gross Weight**	**Net Weight**
52706	0,000	0,000

Batch	**Manufacturing date**	**Expiration date**
2000096166	17.06.2022	17.06.2025

Characteristic	Result	Specification	Unit
Aluminium	< 1	<= 1	ppm
Assay on dried material	100,2	99,0 - 100,5	%(m)
Potassium	54	<= 500	ppm
Barium	Conform test	Conformity	
Magnesium	83	<= 500	ppm
Sodium	24	<= 500	ppm
Lead	< 10	<= 10	ppm
Arsenic	< 3	<= 3	ppm
pH of 5% solution	7,2	7,2 - 8,2	
Readily oxidizable substances	Conform test	Conformity	
Sulphate	< 300	<= 600	ppm
Water	5,7	<= 7,0	%(m)
Chloride	< 40	<= 330	ppm
Iron	< 1,0	<= 20,0	ppm
Fluoride	6	<= 50	ppm
Strontium	117	<= 500	ppm
Nitrate (NO3) (according USP)	Conform test	Conformity	
Appearance	White powder	White powder	
Identification calcium	Conform test	Conformity	
Identification of Acetate	Conform test	Conformity	
Residual Solvents	Conform test	Conformity	
Solubility	Conform test	Conformity	
Appearance of Solution	Clear	Clear	

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Manufacturing date	Expiration date
17.06.2022	17.06.2025

Characteristic	Result	Specification	Unit

Remarks:

This Certificate of Analysis is based on batch specific analysis. Parameters marked with * are not tested for every batch, but these are tested periodically. All our raw materials are obtained from only approved suppliers and match with our raw material specifications according to our ISO 9001 quality management system. Representative samples of each batch are retained for four years and the analysis results of each batch are archived for 10 years. Each sales order is directly linked to (a) batch number(s).

This CoA is only valid when the product is in its original undamaged packaging and when stored under the recommended conditions.

This Certificate of Analysis has been approved electronically and is valid without a signature.

Approved by:
Approved by:
Teamleader Laboratory
Niacet b.v.
H. van den Hurk

Printing date:
22.12.2023

Printing date:
22.12.2023

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Description
CALCIUM ACETATE PO PH 50KG

Code	**Gross Weight**	**Net Weight**
52706	0,000	0,000

Batch	**Manufacturing date**	**Expiration date**
2000104130	27.09.2022	27.09.2025

Characteristic	Result	Specification	Unit
Aluminium	< 1	<= 1	ppm
Assay on dried material	100,1	99,0 - 100,5	%(m)
Potassium	136	<= 500	ppm
Barium	Conform test	Conformity	
Magnesium	52	<= 500	ppm
Sodium	38	<= 500	ppm
Lead	< 10	<= 10	ppm
Arsenic	< 3	<= 3	ppm
pH of 5% solution	7,3	7,2 - 8,2	
Readily oxidizable substances	Conform test	Conformity	
Sulphate	< 300	<= 600	ppm
Water	5,9	<= 7,0	%(m)
Chloride	< 40	<= 330	ppm
Iron	< 1,0	<= 20,0	ppm
Fluoride	6	<= 50	ppm
Strontium	125	<= 500	ppm
Nitrate (NO3) (according USP)	Conform test	Conformity	
Appearance	White powder	White powder	
Identification calcium	Conform test	Conformity	
Identification of Acetate	Conform test	Conformity	
Residual Solvents	Conform test	Conformity	
Solubility	Conform test	Conformity	
Appearance of Solution	Clear	Clear	

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Manufacturing date	Expiration date
27.09.2022	27.09.2025

Characteristic	Result	Specification	Unit

Remarks:

This Certificate of Analysis is based on batch specific analysis. Parameters marked with * are not tested for every batch, but these are tested periodically. All our raw materials are obtained from only approved suppliers and match with our raw material specifications according to our ISO 9001 quality management system. Representative samples of each batch are retained for four years and the analysis results of each batch are archived for 10 years. Each sales order is directly linked to (a) batch number(s).

This CoA is only valid when the product is in its original undamaged packaging and when stored under the recommended conditions.

This Certificate of Analysis has been approved electronically and is valid without a signature.

Approved by:
Approved by:
Teamleader Laboratory
Niacet b.v.
H. van den Hurk

Printing date:
22.12.2023

Printing date:
22.12.2023

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Description
CALCIUM ACETATE PO PH 50KG

Code	**Gross Weight**	**Net Weight**
52706	0,000	0,000

Batch	**Manufacturing date**	**Expiration date**
2000105017	01.11.2022	01.11.2025

Characteristic	Result	Specification	Unit
Aluminium	< 1	<= 1	ppm
Assay on dried material	100,1	99,0 - 100,5	%(m)
Potassium	66	<= 500	ppm
Barium	Conform test	Conformity	
Magnesium	48	<= 500	ppm
Sodium	37	<= 500	ppm
Lead	< 10	<= 10	ppm
Arsenic	< 3	<= 3	ppm
pH of 5% solution	7,3	7,2 - 8,2	
Readily oxidizable substances	Conform test	Conformity	
Sulphate	< 400	<= 600	ppm
Water	6,1	<= 7,0	%(m)
Chloride	< 50	<= 330	ppm
Iron	< 1,0	<= 20,0	ppm
Fluoride	7	<= 50	ppm
Strontium	107	<= 500	ppm
Nitrate (NO3) (according USP)	Conform test	Conformity	
Appearance	White powder	White powder	
Identification calcium	Conform test	Conformity	
Identification of Acetate	Conform test	Conformity	
Residual Solvents	Conform test	Conformity	
Solubility	Conform test	Conformity	
Appearance of Solution	Clear	Clear	

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Manufacturing date	Expiration date
01.11.2022	01.11.2025

Characteristic	Result	Specification	Unit

Remarks:

This Certificate of Analysis is based on batch specific analysis. Parameters marked with * are not tested for every batch, but these are tested periodically. All our raw materials are obtained from only approved suppliers and match with our raw material specifications according to our ISO 9001 quality management system. Representative samples of each batch are retained for four years and the analysis results of each batch are archived for 10 years. Each sales order is directly linked to (a) batch number(s).

This CoA is only valid when the product is in its original undamaged packaging and when stored under the recommended conditions.

This Certificate of Analysis has been approved electronically and is valid without a signature.

Approved by:
Approved by:
Teamleader Laboratory
Niacet b.v.
H. van den Hurk

Printing date:
22.12.2023

Printing date:
22.12.2023

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Description
CALCIUM ACETATE PO PH 50KG

Code	**Gross Weight**	**Net Weight**
52706	0,000	0,000

Batch	**Manufacturing date**	**Expiration date**
2000113251	28.09.2023	28.09.2026

Characteristic	Result	Specification	Unit
Aluminium	< 1	<= 1	ppm
Assay on dried material	99,9	99,0 - 100,5	%(m)
Potassium	131	<= 500	ppm
Barium	Conform test	Conformity	
Magnesium	50	<= 500	ppm
Sodium	36	<= 500	ppm
Lead	< 10	<= 10	ppm
Arsenic	< 3	<= 3	ppm
pH of 5% solution	7,3	7,2 - 8,2	
Readily oxidizable substances	Conform test	Conformity	
Sulphate	< 400	<= 600	ppm
Water	5,9	<= 7,0	%(m)
Chloride	< 50	<= 330	ppm
Iron	< 1,0	<= 20,0	ppm
Fluoride	8	<= 50	ppm
Strontium	127	<= 500	ppm
Nitrate (NO3) (according USP)	Conform test	Conformity	
Appearance	White powder	White powder	
Identification calcium	Conform test	Conformity	
Identification of Acetate	Conform test	Conformity	
Residual Solvents	Conform test	Conformity	
Solubility	Conform test	Conformity	
Appearance of Solution	Clear	Clear	

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Manufacturing date	Expiration date
28.09.2023	28.09.2026

Characteristic	Result	Specification	Unit

Remarks:

This Certificate of Analysis is based on batch specific analysis. Parameters marked with * are not tested for every batch, but these are tested periodically. All our raw materials are obtained from only approved suppliers and match with our raw material specifications according to our ISO 9001 quality management system. Representative samples of each batch are retained for four years and the analysis results of each batch are archived for 10 years. Each sales order is directly linked to (a) batch number(s).

This CoA is only valid when the product is in its original undamaged packaging and when stored under the recommended conditions.

This Certificate of Analysis has been approved electronically and is valid without a signature.

Approved by:
Approved by:
Teamleader Laboratory
Niacet b.v.
H. van den Hurk

Printing date:
22.12.2023

Printing date:
22.12.2023

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Description
CALCIUM ACETATE PO PH 50KG

Code	**Gross Weight**	**Net Weight**
52706	0,000	0,000

Batch	**Manufacturing date**	**Expiration date**
2000100794	19.09.2022	19.09.2025

Characteristic	Result	Specification	Unit
Aluminium	< 1	<= 1	ppm
Assay on dried material	100,2	99,0 - 100,5	%(m)
Potassium	119	<= 500	ppm
Barium	Conform test	Conformity	
Magnesium	70	<= 500	ppm
Sodium	34	<= 500	ppm
Lead	< 10	<= 10	ppm
Arsenic	< 3	<= 3	ppm
pH of 5% solution	7,3	7,2 - 8,2	
Readily oxidizable substances	Conform test	Conformity	
Sulphate	< 300	<= 600	ppm
Water	5,8	<= 7,0	%(m)
Chloride	< 40	<= 330	ppm
Iron	< 1,0	<= 20,0	ppm
Fluoride	5	<= 50	ppm
Strontium	115	<= 500	ppm
Nitrate (NO3) (according USP)	Conform test	Conformity	
Appearance	White powder	White powder	
Identification calcium	Conform test	Conformity	
Identification of Acetate	Conform test	Conformity	
Residual Solvents	Conform test	Conformity	
Solubility	Conform test	Conformity	
Appearance of Solution	Clear	Clear	

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Manufacturing date	Expiration date
19.09.2022	19.09.2025

Characteristic	Result	Specification	Unit

Remarks:

This Certificate of Analysis is based on batch specific analysis. Parameters marked with * are not tested for every batch, but these are tested periodically. All our raw materials are obtained from only approved suppliers and match with our raw material specifications according to our ISO 9001 quality management system. Representative samples of each batch are retained for four years and the analysis results of each batch are archived for 10 years. Each sales order is directly linked to (a) batch number(s).

This CoA is only valid when the product is in its original undamaged packaging and when stored under the recommended conditions.

This Certificate of Analysis has been approved electronically and is valid without a signature.

Approved by:
Approved by:
Teamleader Laboratory
Niacet b.v.
H. van den Hurk

Printing date:
22.12.2023

Printing date:
22.12.2023

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel.info@kerry.com
www.niacet.com

IBAN NL61BOFA0266533965
Trade register Tiel
Registration 11044303
VAT NL807461817B01

Certificate of Analysis

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O.Box 60, 4000 AB Tiel
The Netherlands

MANUFACTURING SITE
Niacet Tiel (MFG)

MATERIAL	20710116	CALCIUM ACETATE AG PH NLI 25KG	
PRINT DATE	22.12.2023*		

BATCH	0007643963	BEST BEFORE DATE/EXPIRY DATE	11.11.2026*
		PRODUCTION DATE	12.11.2023*
		RELEASE DATE	13.11.2023*

INSPECTION CHARACTERISTICS	RESULT	UNITS	SPECIFICATION	
			LOWER	UPPER
Appearance	White agglomerate			
Water	5.1	% mass		7.0
Assay on dried material	100.0	% mass	99.0	100.5
Chloride	< 40	ppm		500
Sulphate	< 300	ppm		600
Potassium	116	ppm		500
Sodium	31	ppm		5000

BATCH	0007643963	BEST BEFORE DATE/EXPIRY DATE	11.11.2026*
		PRODUCTION DATE	12.11.2023*
		RELEASE DATE	13.11.2023*

Magnesium	34	ppm		500
Aluminium	< 1	ppm		2
pH of 5% solution	7.5		6.3	9.6
Sulphate	< 3	ppm		3
Fluoride	7	ppm		50
Lead	< 10	ppm		10
Readily oxidizable substances	Conform			
Strontium	122	ppm		500
Nitrate	Conform			
Barium	Conform			
Identification of Acetate	Conform			
Identification calcium	Conform			
Residual Solvents	Conform			
Bulk density (USP BD method 1)	0.66	g/mL	0.60	
Particle size (>1000u)	0.0	% mass		1.0
Tapped density (USP TD method 1)	0.74	g/mL	0.70	

BATCH	0007643963	BEST BEFORE DATE/EXPIRY DATE	11.11.2026*
		PRODUCTION DATE	12.11.2023*
		RELEASE DATE	13.11.2023*

This Certificate of Analysis is based on batch specific analysis. Parameters marked with * are not tested for every batch, but these are tested periodically. All our raw materials are obtained from only approved suppliers and match with our raw material specifications according to our ISO 9001 quality management system. Representative samples of each batch are retained for four years and the analysis results of each batch are archived for 10 years. Each sales order is directly linked to (a) batch number(s).

This CoA is only valid when the product is in its original undamaged packaging and when stored under the recommended conditions.

This Certificate of Analysis has been approved electronically and is valid without a signature.

The product described in this certificate has been manufactured and tested in accordance with our standard procedures applicable to such product and conforms to the specifications for such product set forth herein.

Unless we have agreed to provide per batch or other testing frequency (in which case conformity has been determined in accordance with our contractual agreement), conformity to specification has been determined based on our risk assessment and our periodic, statistically-based testing program for the product.

All information appearing in this certificate is based upon tests and data we deem reliable. It is the customer's responsibility to determine the suitability of the product for its own use(s) and appropriate shipping, packaging, storage and/or distribution conditions, and no representation, warranty or guarantee, express or implied, is made by us in this certificate as to the suitability or effect of such use(s) or results to be obtained under actual use by customer or other third parties.

*All dates in this document are expressed in the format DD.MM.YYYY

Niacet
400 47th Street
Niagara Falls, NY 14304
USA

T + 1 716 285 1474

www.niacet.com

Kaiping Deng, Ph.D.
Division of Food Ingredients
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD
20740-3835 USA

January 29,2024

Re: GRAS Notice No. GRN 001126

Dear Dr. Deng,

Please see the below responses to the United States (U.S.) Food and Drug Administration (FDA)'s letter dated January 11th, 2024 pertaining to information provided within Niacet's Generally Recognized as Safe (GRAS) Notice for calcium acetate filed by the Agency under GRN 001126.

FDA.1. *In the response to question 4 of the FDA questions dated November 2, 2023, Niacet presents results for the analysis of calcium acetate for arsenic and lead and notes a maximum specification based on ICH Q3D(R1) guidelines for arsenic and lead of <1.5 mg/kg and <0.5 mg/kg, respectively (2023-12-07 Amendment 2a).*

a) Please confirm that Niacet is amending the limits for arsenic and lead for calcium acetate in GRN 001126.
b) Please provide the analytical method used for the analysis of calcium acetate for arsenic and lead.
c) Additionally, Niacet provides results from only one batch analyses to support the updated specification. Please provide results from two additional non-consecutive batch analyses for arsenic and lead.
d) We note that specifications for heavy metals should be as low as possible and reflective of the results from the batch analyses. Please consider reducing the specifications for the heavy metals.

Niacet Response: Analytical data for arsenic and lead conducted using a more sensitive test method to that described in the Food Chemicals Codex (11th Edition) was presented in response to the FDA's request which stated the following:

"*Please provide results from more sensitive methods such as FDA EAM 4.7 or AOAC 2015.01*".

The certificate of analysis provided to the FDA was for product (calcium acetate) intended for use in pharmaceutical applications; however, the production process for the pharmaceutical grade *vs*. food grade material are identical. This data was presented to demonstrate that Niacet's production process produces an ingredient of high quality that is absent heavy metal contamination. Although Niacet concedes that product produced by the company for food use applications would consistently meet the lower heavy metal specifications set-forth for the pharma grade product, the company will comply with the food grade specifications for calcium acetate set forth in the most recent version of the Food Chemicals Codex. Extended testing requirements for calcium acetate outside of those specified in the Food Chemicals Codex would place Niacet at a commercial disadvantage as this would create a company specific testing burden that its competitors would not be beholden to. Niacet recognizes the importance of the FDA's closer to zero initiative and believes that its ingredients are compliant with this mandate as is evidence by the low levels of lead and arsenic reported in the certificate of analysis that was provided to the agency.

FDA.2. *In the amendment dated August 16, 2023, Niacet stated that the intended uses of calcium acetate will be partially substitutional for calcium propionate as the use level to achieve the technical effect for calcium acetate is higher (0.5%) compared to calcium propionate (0.3%). Therefore, this will result in a higher dietary exposure for calcium from the proposed substitution of calcium propionate for calcium acetate. In the same amendment, Niacet noted that the majority of calcium consumed in the diet is*

from natural sources and dietary supplements which poses a limitation to estimating dietary exposure to calcium among the high consumers (e.g., 90th percentile). Thus, Niacet proposed using the NCI method for estimating dietary exposure to more accurately model the intake of calcium. FDA estimated the dietary exposure to calcium using the NCI method using data from 2015-2017 National Health and Examination Survey (NHANES). For males and females aged 51-70 years and for those individuals over 71 years (combined male and female) FDA estimated background dietary exposures (food and dietary supplements) to calcium at the 90th percentile to be 1678 mg/p/d, 1640 mg/p/d, and 1634 mg/p/d, respectively. For the cumulative dietary exposure to calcium (background intake and the proposed increase due to the partially substitutional uses, see above), using the same method and same subpopulations, FDA estimated the dietary exposure to calcium to be 1873 mg/p/d, 1761 mg/p/d, and 1784 mg/p/d. Does Niacet concur with the dietary exposures estimated by FDA for calcium?

Niacet thanks the FDA for taking the time to conduct these intake estimates and agrees that the agency's estimations seem reasonable.

We also would like to thank the FDA for their patience, and diligent review of the company's proposed GRAS uses of calcium acetate in food and believe that our responses to the agency's questions will address the FDA's final outstanding points.

Sincerely,

Salvatore J. D'Angelo
Consultant, Quality Assurance & Regulatory Affairs

Niacet Corporation A Kerry Company
400 47th Street
Niagara Falls, NY 14304

Niacet A Kerry Company 400 47th Street Niagara Falls, NY 14304 716-285-1474

April 05,2024

Kaiping Deng, Ph.D.
Division of Food Ingredients
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD
20740-3835 USA

Re: GRAS Notice No. GRN 001126

Dear Dr. Deng,

Please see the below responses to the United States (U.S.) Food and Drug Administration (FDA)'s questions pertaining to Niacet's Generally Recognized as Safe (GRAS) Notice for calcium acetate filed by the Agency under GRN 001126.

FDA.1. *According to §170.3(o)(2), "Antimicrobial agents: Substances used to preserve food by preventing growth of microorganisms and subsequent spoilage, including fungistats, mold and rope inhibitors, and the effects listed by the National Academy of Sciences/National Research Council under 'preservatives'." On page 4, Niacet states that "Calcium acetate is used in the following foods as an antimicrobial agent at levels not to exceed current good manufacturing practices (cGMP): baked goods; cheeses; confections and frostings; gelatins, puddings, and fillings; and jams and jellies. These food uses are fully substitutional to the current GRAS uses of calcium propionate under 21 CFR § 184.1221 (U.S. FDA, 2021)."*

Please specify the microorganisms that calcium acetate is intended to target in each of the food category, and provide additional data to support the use of the ingredient as an antimicrobial agent.

Niacet Response:

Calcium acetate is an effective growth inhibitor of many bacteria and molds. It is widely employed in bread and other bakery products to extend shelf-life and to prevent rope formation. The high moisture content of bakery goods encourages the growth of molds and rope bacteria. Rope spoilage is characterized by a sticky, wet, and brownish crumb as well as an unpleasant smell. Rope forming bacteria and many mold spores are heat resistant and survive the temperatures of the baking process. Bacteria responsible for ropy spoilage include *Bacillus amyloliquefaciens*, *B. subtilis*, *B. licheniformis*, the *B. cereus* group, *B. pumilus*, *B. sonorensis*, *Cytobacillus firmus*, *Niallia circulans*, *Paenibacillus polymyxa*, and *Priestia megaterium* (Pacher *et al*., 2022). Acetate salts have been used for over a century for control of rope bacteria in various food types (Watkins, 1906; Cook et al., 2009; Alex et al., 2017). This long history of use of calcium acetate as a general preservative in food is reflected in the JECFA monograph for calcium acetate where it is referenced as an antimold and antirope agent (JECFA, 1973) and the listing of calcium acetate as suitable for use as a preservative in the CODEX Alimentarius GSFA provisions tables that include all aforementioned food uses referenced by the U.S. FDA. As Niacet is a supplier of food ingredient and not a food manufacturer, the specific conditions of use in each food category are determined on a case-by-case basis the by each manufacturer and are determined by

the type of food processing conditions, and potential synergistic use of other preservatives/antimicrobial treatments that are permitted for food use and available to the manufacturer. For example, as reported by Zhitnitsky *et al*., (2017) highly synergistic, broad spectrum, antibacterial activity of organic acids can be attained in the presence of transition metals, and patents for the use of calcium acetate as an antimicrobial can be identified that reference the effectiveness of this substances against various food spoilage and pathogenic organisms[1]. The focus of the GRAS conclusion is on safety and the particular methods used by each manufacturer to obtain optimal utility are always case by case and can be proprietary in nature. Niacet also notes that data and information provided in support of the utility of calcium acetate as a preservative are aligned with the standards established in previous GRAS conclusions for 'natural preservative' substances with a long-history of safe use such as citrus fruit extract under GRN 475.

GSFA Table 3 Provisions

Calcium acetate is a food additive that is included in **Table 3**, and as such may be used in the following foods under the conditions of good manufacturing practices (GMP) as outlined in the Preamble of the Codex GSFA. Although not listed below, Calcium acetate could also be used in heat-treated butter milk of food category 01.1.1 and spices of food category 12.2.1. Note that food categories listed in the **Annex to Table 3** were excluded accordingly. **Calcium acetate** is acceptable in foods conforming to the following commodity standards: CS 273-1968, CS 275-1973, CS 262-2006 (for use in cheese mass only), CS 290-1995.

Calcium acetate is a: Acidity regulator, Preservative, Stabilizer

Any Acidity regulator listed in Table 3 can be acceptable for use in all products conforming to CS 117-1981, CS 309R-2011, CS 291-2010, CS 319-2015, CS 256-2007, CS 306-2011.

Any Preservative listed in Table 3 can be acceptable for use in all products conforming to CS 117-1981, CS 291-2010, CS 256-2007, CS 306-2011.

Any Stabilizer listed in Table 3 can be acceptable for use in all products conforming to CS 117-1981, CS 256-2007.

Number	Food Category
01.1.4	Flavoured fluid milk drinks
01.3	Condensed milk and analogues (plain)
01.4.3	Clotted cream (plain)
01.4.4	Cream analogues
01.5	Milk powder and cream powder and powder analogues (plain)
01.6.1	Unripened cheese
01.6.2	Ripened cheese
01.6.4	Processed cheese
01.6.5	Cheese analogues

[1] "Calcium acetate is an excellent bacteriostatic property derived from both acetic acid and calcium, and a tissue-strengthening agent for proteins and cellulose derived from the binding property of calcium, which is a divalent ion. (Effect) can be used very preferably. Calcium acetate, although to varying degrees, has a wide range of bacteriostatic (growth-inhibiting power) against various bacteria, sputum, and yeast that cause food deterioration and food poisoning. Specifically, Gram-positive bacteria such as Bacillus subtilis, Staphylococcus aureus, lactic acid bacteria (genus Lactobacillus, Bifidobacterium, Enterococcus, Lactococcus, etc.), various pathogenic Escherichia coli, Salmonella, Listeria, Campylobacter Negative bacteria, various varieties (Aspergillus, Penicillium, Eurotium, etc.), yeast (Rhodotorula, Saccharomyces rosei, Brettanomyces intermedius, etc.), especially proliferating in refrigerators due to strong low-temperature resistance. It is characterized by high bacteriostatic properties against increasing Listeria monocytogenes and against Salmonella causing severe food poisoning." (https://patents.google.com/patent/JP6228376B2/en).

	Number	Food Category
	01.7	Dairy-based desserts (e.g. pudding, fruit or flavoured yoghurt)
	01.8.1	Liquid whey and whey products, excluding whey cheeses
	02.2.2	Fat spreads, dairy fat spreads and blended spreads
	02.3	Fat emulsions mainly of type oil-in-water, including mixed and/or flavoured products based on fat emulsions
	02.4	Fat-based desserts excluding dairy-based dessert products of food category 01.7
	03.0	Edible ices, including sherbet and sorbet
	04.1.2	Processed fruit
	04.2.2.2	Dried vegetables (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera), seaweeds, and nuts and seeds
	04.2.2.3	Vegetables (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera), and seaweeds in vinegar, oil, brine, or soybean sauce
	04.2.2.4	Canned or bottled (pasteurized) or retort pouch vegetables (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera), and seaweeds
	04.2.2.5	Vegetable (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera), seaweed, and nut and seed purees and spreads (e.g., peanut butter)
	04.2.2.6	Vegetable (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera), seaweed, and nut and seed pulps and preparations (e.g. vegetable desserts and sauces, candied vegetables) other than food category 04.2.2.5
	04.2.2.8	Cooked or fried vegetables (including mushrooms and fungi, roots and tubers, pulses and legumes, and aloe vera), and seaweeds
	05.0	Confectionery
	06.3	Breakfast cereals, including rolled oats
	06.4.3	Pre-cooked pastas and noodles and like products
	06.5	Cereal and starch based desserts (e.g. rice pudding, tapioca pudding)
	06.6	Batters (e.g. for breading or batters for fish or poultry)
	06.7	Pre-cooked or processed rice products, including rice cakes (Oriental type only)
	06.8	Soybean products (excluding soybean-based seasonings and condiments of food category 12.9)
	07.0	Bakery wares
	08.2	Processed meat, poultry, and game products in whole pieces or cuts
	08.3	Processed comminuted meat, poultry, and game products
	08.4	Edible casings (e.g. sausage casings)
	09.3	Semi-preserved fish and fish products, including mollusks, crustaceans, and echinoderms
	09.4	Fully preserved, including canned or fermented fish and fish products, including mollusks, crustaceans, and echinoderms

Number	Food Category
10.2.3	Dried and/or heat coagulated egg products
10.3	Preserved eggs, including alkaline, salted, and canned eggs
10.4	Egg-based desserts (e.g. custard)
11.6	Table-top sweeteners, including those containing high-intensity sweeteners
12.2.2	Seasonings and condiments
12.3	Vinegars
12.4	Mustards
12.5	Soups and broths
12.6	Sauces and like products
12.7	Salads (e.g. macaroni salad, potato salad) and sandwich spreads excluding cocoa- and nut-based spreads of food categories 04.2.2.5 and 05.1.3
12.8	Yeast and like products
12.9	Soybean-based seasonings and condiments
12.10	Protein products other than from soybeans
13.3	Dietetic foods intended for special medical purposes (excluding products of food category 13.1)
13.4	Dietetic formulae for slimming purposes and weight reduction
13.5	Dietetic foods (e.g. supplementary foods for dietary use) excluding products of food categories 13.1 - 13.4 and 13.6
13.6	Food supplements
14.1.4	Water-based flavoured drinks, including "sport," "energy," or "electrolyte" drinks and particulated drinks
14.2.1	Beer and malt beverages
14.2.2	Cider and perry
14.2.4	Wines (other than grape)
14.2.5	Mead
14.2.6	Distilled spirituous beverages containing more than 15% alcohol
14.2.7	Aromatized alcoholic beverages (e.g. beer, wine and spirituous cooler-type beverages, low alcoholic refreshers)
15.0	Ready-to-eat savouries
16.0	Prepared foods

In addition to the above response, Niacet would like to reconsider its specifications for heavy metals in light of the U.S. FDA's closer to zero initiative. Accordingly, Niacet is reducing the specification for lead from 2 ppm to 0. 5 ppm, arsenic from 3 to 1.5 ppm and a specification for mercury will be set at 0.1 ppm (See Attachment 1 fo a copy of the revised product specifications).

We thank the FDA for their patience, and diligent review of the company's proposed GRAS uses of calcium acetate in food and believe that our responses to the agency's questions will address the FDA's final outstanding points.

Sincerely,

Salvatore J. D'Angelo

Niacet, A Kerry Company
400 47th Street
Niagara Falls, NY 14304

References

Axel, C.; Zannini, E.; Arendt, E.K (2017). Mold spoilage of bread and its bio preservation: A review of current strategies for bread shelf-life extension. Crit. Rev. Food Sci. Nutr. 57:3528–3542.

Cook, F.K. and Johnson, B.L. Microbiological Spoilage of Cereal Products (2009). In Compendium of the Microbiological Spoilage of Foods and Beverages; Sperber, W.H., Doyle, M.P., Eds.; Springer: New York, NY, USA; London, UK. Pp. 223–244.

Pacher, N.; Burtscher, J.; Johler, S.; Etter, D.; Bender, D.; Fieseler, L.; Domig, K.J (2022). Ropiness in Bread—A Re-Emerging Spoilage Phenomenon. Foods. 11:3021.

Watkins, E.J (1906). Ropiness in flour and bread and its detection and prevention. J. Soc. Chem. Ind. 25: 350–357.

Zhitnitsky, D., Rose, J. & Lewinson, O (2017). The highly synergistic, broad spectrum, antibacterial activity of organic acids and transition metals. Sci Rep. 7:44554.

Progusta CA

Calcium acetate food grade

SPECIFICATIONS	CONTROL LIMITS
Appearance	White granules or powder
Assay on dried material	99.0 – 100.5 % mass
Water	≤ 6.0 % mass
Insoluble in water	≤ 0.1 % mass
Chloride (Cl^-)	≤ 0.05 % mass
Fluoride (F^-)	≤ 0.005 % mass
Sulphate (SO_4^-)	≤ 0.1 % mass
Iron (Fe)	≤ 10 ppm
Arsenic (As)	< 1.5 ppm
Lead (Pb)	< 0.5 ppm
Mercury (Hg)	< 0.1 ppm
Oxidizable impurities	≤ 0.1 % mass (as formic acid)
pH of 10% solution	6.0 - 9.0

Food grade conforms to the latest FCC, E263 JECFA (FAO/WHO) and Japanese Standards of Food Additives..
For more detailed information please see Technical Data Sheet and Safety Data Sheet. This product is currently produced in the Netherlands.

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O. Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel@niacet.nl
www.niacet.com

NIACET A Kerry Company 400 47th Street Niagara Falls, NY 14304 716-285-1474

April 19,2024

Kaiping Deng, Ph.D.
Division of Food Ingredients
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD
20740-3835 USA

Re: GRAS Notice No. GRN 001126

Dear Dr. Deng,

Please see the below responses to questions outlined in the United States (U.S.) Food and Drug Administration (FDA)'s request for information (RFI) letter dated April 12, 2024 pertaining to Niacet's Generally Recognized as Safe (GRAS) Notice for calcium acetate filed by the Agency under GRN 001126.

FDA.1. *Niacet states that the calcium acetate specifications for lead, arsenic and mercury are reduced to 0.5 mg/kg, 1.5 mg/kg and 0.1 mg/kg, respectively. Please provide the results from the analyses of two additional non-consecutive batches for lead, arsenic, and mercury to ensure that calcium acetate can be produced according to the specifications.*

Niacet Response:

Certificates of analyses for two additional non-consecutive batches containing analytical data for lead, arsenic, and mercury are provided as attachments. All lots of material demonstrate compliance with Niacet's revised specification for these metals.

FDA.2. *We appreciate the information of calcium acetate controlling rope forming bacteria and mold spores in baked goods. However, since there is no publicly available data for pathogen control, we suggest Niacet limit the intended technical effect to spoilage microorganisms.*

Niacet Response:

Niacet agrees that in the absence of publicly available data for pathogen control that the intended conditions of use in food should be limited to control of spoilage microorganisms.

We thank the agency for their efforts in evaluating Niacet's GRAS notification and believe that our responses to the agency's questions will address the FDA's final outstanding points.

Sincerely,

Salvatore J. D'Angelo
Niacet, A Kerry Company
400 47th Street Niagara Falls NY 14304

Laboratory report

NutriControl-2024013650-V01

NutriControl
analytical solutions

N.C.B. laan 52
5462 GE Veghel

Postbus 107
5460 AC Veghel

T [+31] 413 38 26 33

info@nutricontrol.nl
www.nutricontrol.nl

Niacet b.v.
attn. Pieter Timmermans
Postbus 60
4000 AB TIEL

Sample number	:	M24002625018
Customer number	:	D05359
Date Sample received	:	31-01-2024
Digital order ID	:	NC000158551018

Your sample characteristics

Subject	:	Annual undesirable substances
Productname	:	Calcium Acetate
External code	:	9010958734
Product code customer	:	/
Additional info	:	/
Sampling date	:	29-7-2023
Cost code	:	7101705422

Parameter	Result	Target	Unit	Method	Accr./cert.
Fluoride	<20	20	mg/kg	10012	Q G-B10
Arsenic (As)	<0,200	1,000	mg/kg	10222	Q G-B11 QS
Cadmium (Cd)	<0,100	0,100	mg/kg	10222	Q G-B11 QS
Mercury (Hg)	<0,100	0,100	mg/kg	10222	Q G-B10 QS
Lead (Pb)	<0,200	2,000	mg/kg	10222	Q G-B11 QS

Pieter Timmermans
Digitally signed by Pieter Timmermans
Date: 2023.02.09 13:55:26 +01'00'

Manager Analytical Services, H.J.M. Lamers, Veghel, 08-02-2023

Laboratory report

NutriControl-2023015532-V01

NutriControl
analytical solutions

N.C.B. laan 52
5462 GE Veghel

Postbus 107
5460 AC Veghel

T [+31] 413 38 26 33

info@nutricontrol.nl
www.nutricontrol.nl

Niacet b.v.
attn. Pieter Timmermans
Postbus 60
4000 AB TIEL

Sample number	:	M23003031011
Customer number	:	D05359
Date Sample received	:	31-01-2023
Digital order ID	:	NC000134613011

Your sample characteristics

Subject	:	Yearly undesirable substances (2023)
Productname	:	Calcium Acetate
External code	:	2000105626
Product code customer	:	/
Additional info	:	/
Sampling date	:	12-10-2022
Cost code	:	4300001830

Parameter	Result	Target	Unit	Method	Accr./cert.
Fluoride	<20	20	mg/kg	10012	Q G-B10
Arsenic (As)	<0,200		mg/kg	10222	Q G-B11 QS
Cadmium (Cd)	<0,100		mg/kg	10222	Q G-B11 QS
Mercury (Hg)	<0,100		mg/kg	10222	Q G-B10 QS
Lead (Pb)	<0,200		mg/kg	10222	Q G-B11 QS

Pieter Timmermans
Digitally signed by Pieter Timmermans
Date: 2024.02.16 11:55:22 +01'00'

Manager Analytical Services, A. Loete,
Veghel, 15-02-2024

Q = accredited by Raad voor Accreditatie EN/ISO/IEC 17025 (certificate L053), (Q' by given certificate number), G-B10 = certified according to GMP+(-B11 Feed Safety Assurance), QS = approved by QS, External = subcontracted, * = indicative value, "" = microorganisms present/gram, a = additional test, r = reanalysis, (D) = average duplo.

The analysis is performed in the period between the date of sample receipt at NutriControl and the date of reporting. Microbiological analysis of perishable products is started within 24 hours of samples receipt, unless otherwise stated. The analytical results are valid for the delivered sample material only. Information about measurement uncertainty and source energy value can be delivered on request. General terms and conditions apply to all services and the supply of goods and products. These can be found on www.nutricontrol.nl. If the reportnumber contains V2 or higher, then this report replaces the previous report. Without the permission of NutriControl, this report may only be copied integral.

NIACET A Kerry Company 400 47th Street Niagara Falls, NY 14304 716-285-1474

Kaiping Deng, Ph.D.
Division of Food Ingredients
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD
20740-3835 USA

April 26, 2024

Re: GRAS Notice No. GRN 001126

Dear Dr. Deng,

Please see the below responses to the United States (U.S.) Food and Drug Administration (FDA)'s questions pertaining to Niacet's Generally Recognized as Safe (GRAS) Notice for calcium acetate filed by the Agency under GRN 001126.

FDA.1. *In the amendment dated April 5, 2024, Niacet reduced the specifications for lead, arsenic and mercury to 0.5 mg/kg, 1.5 mg/kg and 0.1 mg/kg, respectively. In the amendment dated April 19, 2024, Niacet presented results from the analyses of additional batches for lead, arsenic and mercury that showed that calcium acetate can be produced with a lead, arsenic and mercury level of < 0.2 mg/kg, <0.2 mg/kg and <0.1 mg/kg, respectively. Please reconsider further reducing the specification for arsenic and lead to reflect the batch analyses presented in the amendments dated December 7, 2023 and April 24, 2024.*

Niacet Response:

Niacet agrees with the FDA's request to reconsider the proposed specifications for lead and arsenic. Accordingly, Niacet is reducing the specification for lead from <0.5 ppm to <0.2 ppm and the specification for arsenic will be reduced from <1.5 ppm to <0.2 ppm. (See Attachment 1 for a copy of the revised product specification).

We thank the FDA for their patience, and diligent review of the company's proposed GRAS uses of calcium acetate in food and believe that our responses to the agency's questions will address the FDA's final outstanding points.

Sincerely,

Salvatore J. D'Angelo
Niacet, A Kerry Company
400 47th Street Niagara Falls, NY 14304

Progusta CA

Calcium acetate food grade

SPECIFICATIONS	CONTROL LIMITS
Appearance	White granules or powder
Assay on dried material	99.0 – 100.5 % mass
Water	≤ 6.0 % mass
Insoluble in water	≤ 0.1 % mass
Chloride (Cl^-)	≤ 0.05 % mass
Fluoride (F^-)	≤ 0.005 % mass
Sulphate (SO_4^-)	≤ 0.1 % mass
Iron (Fe)	≤ 10 ppm
Arsenic (As)	<0.2 ppm
Lead (Pb)	< 0.2 ppm
Mercury (Hg)	< 0.1 ppm
Oxidizable impurities	≤ 0.1 % mass (as formic acid)
pH of 10% solution	6.0 - 9.0

Food grade conforms to the latest FCC, E263 JECFA (FAO/WHO) and Japanese Standards of Food Additives..
For more detailed information please see Technical Data Sheet and Safety Data Sheet. This product is currently produced in the Netherlands.

Niacet b.v.
Papesteeg 91, 4006 WC Tiel
P.O. Box 60, 4000 AB Tiel
The Netherlands

Tel. +31 344 615 224
Fax +31 344 611 475
tiel@niacet.nl
www.niacet.com