

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

28 AUG 2019

Applicant's or agent's file reference
5419520150490

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US2019/038948

International filing date (day/month/year)

25 June 2019

Priority date (day/month/year)

International Patent Classification (IPC) or both national classification and IPC

IPC(8) - A23L 33/155; A23L 33/00; A61K 31/19; A61K 31/59; C07C 65/00 (2019.01)

CPC - A23L 33/155; A23L 33/00; A23L 33/15; A23V 2002/00; A61K 31/19; A61K 31/198; A61K 31/59 (2019.08)

Applicant METABOLIC TECHNOLOGIES, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis. I(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US
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Facsimile No. 571-273-8300

Date of completion of this opinion

05 August 2019

Authorized officer

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**WRITTEN OPINION OF THE
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed.
 - ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a)).
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2, 3, 7, 10	YES
	Claims	1, 4-6, 8, 9	NO
Inventive step (IS)	Claims	None	YES
	Claims	1-10	NO
Industrial applicability (IA)	Claims	1-10	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1, 4-6, 8, and 9 lack novelty under PCT Article 33(2) as being anticipated by Abbott Laboratories (hereinafter Abbott).

Regarding claim 1, Abbott discloses a stable formulation comprising β -hydroxy- β -methylbutyrate (HMB) in the free acid form (Para.[0043] and Para.[0044]. The nutritional products comprise HMB..... HMB as the free acid), vitamin D (Para.[0072]. The products may further comprise vitamins or related nutrients, non-limiting examples of which include...vitamin D) and at least one stabilizing excipient (Para.[0071]. Non-limiting examples of such optional ingredients include...stabilizers).

Regarding claim 4, Abbott discloses the formulation of claim 1, wherein the formulation is contained within a delivery form selected from the list consisting of a capsule, a softgel, a liquid, and a foodstuff. (Para.[0032]. The nutritional products include nutritional liquids and nutritional solid forms, which include emulsified liquids, powders, including dry-mixed and/or spraydried powders that can be diluted with water or other aqueous liquids to form a nutritional liquid prior to use, nutritional bars and the like).

Regarding claim 5, Abbott discloses a method of stabilizing vitamin D in an acidic formulation (Para.[0043] and Para.[0044]. The nutritional products comprise HMB..... HMB as the free acid; Para.[0071]. Non-limiting examples of such optional ingredients include...stabilizers; Para.[0072]. The products may further comprise vitamins or related nutrients, non-limiting examples of which include...vitamin D), comprising the step of including at least one stabilization excipient in a formulation containing vitamin D and β -hydroxy- β -methylbutyrate (HMB) form (Para.[0043] and Para.[0044]; Para. [0071; Para. [0072]).

Regarding claim 6, Abbott discloses the method of claim 5, wherein the HMB is the free acid form (Para.[0043] and Para.[0044]. The nutritional products comprise HMB..... HMB as the free acid).

Regarding claim 8, Abbott discloses a method of minimizing degradation of vitamin D in an acidic formulation containing β -hydroxy- β -methylbutyrate (HMB) (Para.[0043] and Para.[0044]. The nutritional products comprise HMB..... HMB as the free acid; Para.[0071]. Non-limiting examples of such optional ingredients include...stabilizers; Para.[0072]. The products may further comprise vitamins or related nutrients, non-limiting examples of which include...vitamin D) comprising the step of including at least one stabilization excipient in said formulation (Para.[0043] and Para.[0044]; Para. [0071; Para. [0072]).

Regarding claim 9, Abbott discloses the method of claim 8, wherein the HMB is the free acid form. (Para.[0043] and Para.[0044]. The nutritional products comprise HMB..... HMB as the free acid).

Claims 2, 3, 7, and 10 lack an inventive step under PCT Article 33(3) as being obvious over Abbott Laboratories (hereinafter Abbott) in view of Boardman et al. (hereinafter Boardman).

Regarding claim 2, Abbott discloses the formulation of claim 1. Abbott fails to explicitly disclose the formulation of claim 1, wherein the stabilizing excipient is selected from the list consisting of EDTA, butylated hydroxytoluene (BHT), carnitine, rosemary extract, carnosolic acid, and sorbic acid. However, Boardman is in the field of Process for preparing stabilized Vitamin D (Boardman, Title) and teaches wherein the stabilizing excipient is selected from the list consisting of EDTA, butylated hydroxytoluene (BHT), carnitine, rosemary extract, carnosolic acid, and sorbic acid (Boardman, Para.[0034]. Examples of antioxidants include, but are not limited to, vitamin A, vitamin C, vitamin E (tocopherol), butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), propyl gallate (PG), hydroquinone, α -tocopherol, ascorbic acid, ascorbyl palmitate, vitamin E palmitate, sodium bisulfite, ethylenediaminetetraacetic acid (EDTA), combinations thereof, and the like. In an embodiment, the antioxidant is ascorbyl palmitate, BHA, PG, BHT, EDTA, sodium bisulfite or combinations thereof. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the composition of Abbott with the teaching of Boardman for the purpose to reduce the rate of degradation of vitamin D3 (Boardman, Para. [0001]).

Regarding claim 3, Abbott discloses the formulation of claim 1. Abbott fails to explicitly disclose wherein the stabilizing excipient is selected from the list consisting of EDTA and butylated hydroxytoluene (BHT). Boardman further teaches wherein the stabilizing excipient is selected from the list consisting of EDTA and butylated hydroxytoluene (BHT) (Boardman, Para.[0034]. In another embodiment, the antioxidant is butylated hydroxytoluene (BHT), propyl gallate (PG), ethylenediamine-tetraacetic acid (EDTA), or combinations thereof. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the composition of Abbott with the teaching of Boardman for the purpose to reduce the rate of degradation of vitamin D3 (Boardman, Para. [0001]).

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Regarding claim 7, Abbott discloses the method of claim 5. Abbott fails to explicitly disclose wherein the stabilizing excipient is selected from the list consisting of EDTA, butylated hydroxytoluene (BHT), carnitine, rosemary extract, carnosolic acid, and sorbic acid. Boardman further teaches wherein the stabilizing excipient is selected from the list consisting of EDTA, butylated hydroxytoluene (BHT), carnitine, rosemary extract, carnosolic acid, and sorbic acid. (Boardman, Para. [0034], Examples of antioxidants include, but are not limited to, vitamin A, vitamin C, vitamin E (tocopherol), butylated hydroxytoluene (BHT), butylated hydroxyanisol (BHA), propyl gallate (PG), hydroquinone, α -tocopherol, ascorbic acid, ascorbyl palmitate, vitamin E palmitate, sodium bisulfite, ethylenediaminetetraacetic acid (EDTA), combinations thereof, and the like. In an embodiment, the antioxidant is ascorbyl palmitate, BHA, PG, BHT, EDTA, sodium bisulfite or combinations thereof). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Abbott with the teaching of Boardman for the purpose to reduce the rate of degradation of vitamin D3 (Boardman, Para. [0001]).

Regarding claim 10, Abbott discloses the method of claim 8. Abbott fails to explicitly disclose wherein the stabilizing excipient is selected from the list consisting of EDTA, butylated hydroxytoluene (BHT), carnitine, rosemary extract, carnosolic acid, and sorbic acid. Boardman further teaches wherein the stabilizing excipient is selected from the list consisting of EDTA, butylated hydroxytoluene (BHT), carnitine, rosemary extract, carnosolic acid, and sorbic acid. (Boardman, Para. [0034], Examples of antioxidants include, but are not limited to, vitamin A, vitamin C, vitamin E (tocopherol), butylated hydroxytoluene (BHT), butylated hydroxyanisol (BHA), propyl gallate (PG), hydroquinone, α -tocopherol, ascorbic acid, ascorbyl palmitate, vitamin E palmitate, sodium bisulfite, ethylenediaminetetraacetic acid (EDTA), combinations thereof, and the like. In an embodiment, the antioxidant is ascorbyl palmitate, BHA, PG, BHT, EDTA, sodium bisulfite or combinations thereof). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Abbott with the teaching of Boardman for the purpose to reduce the rate of degradation of vitamin D3 (Boardman, Para. [0001]).

Claims 1-10 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.