

GREEN BOOK 4

Stearyl Heptanoate

CIR EXPERT PANEL MEETING
JUNE 28-29, 2010

Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons

From: Monice M. Fiume *MMF*
Scientific Analyst/Writer

Date: June 28, 2010

Subject: Stearyl Heptanoate Draft Amended Report

In 1995, the CIR Expert Panel published the Final Report on the Safety Assessment of Stearyl Heptanoate, which concluded that this ingredient is “safe for use as a cosmetic ingredient in the present practices of use.” No new data were found during a search of the literature published since the original report was issued.

The Panel was informed that similar stearyl alkanoates (esters of stearyl alcohol and a fatty acid) are used in cosmetics. At the April 2010 meeting, the Panel agreed that the data contained in the 1995 assessment on Stearyl Heptanoate would be applicable to these additional stearyl alkanoates. A rereview of Stearyl Heptanoate was initiated to include Stearyl Caprylate, Stearyl Palmitate, Stearyl Stearate, Stearyl Behenate, and Stearyl Oliviate.

Since no new data were available, data from the 1995 assessment of stearyl heptanoate were summarized and included in the rereview document. The 1995 assessment included data from the safety assessment on stearyl alcohol; that data are summarized in this report. In looking at the components of the stearyl alkanoates that have been added to this report, it was noted that palmitic and stearic acid have been reviewed by CIR. Data from these reports have been summarized in the report. *All data from previous safety assessments are italicized in this report.*

The Personal Care Products Council conducted an industry survey regarding the concentration of use of these ingredients. That survey has been completed and is included.

Reports and Data available Online (reference in draft amended report):

<http://www.cir-safety.org/jun10.shtml>

Final Report on the Safety Assessment of Stearyl Heptanoate

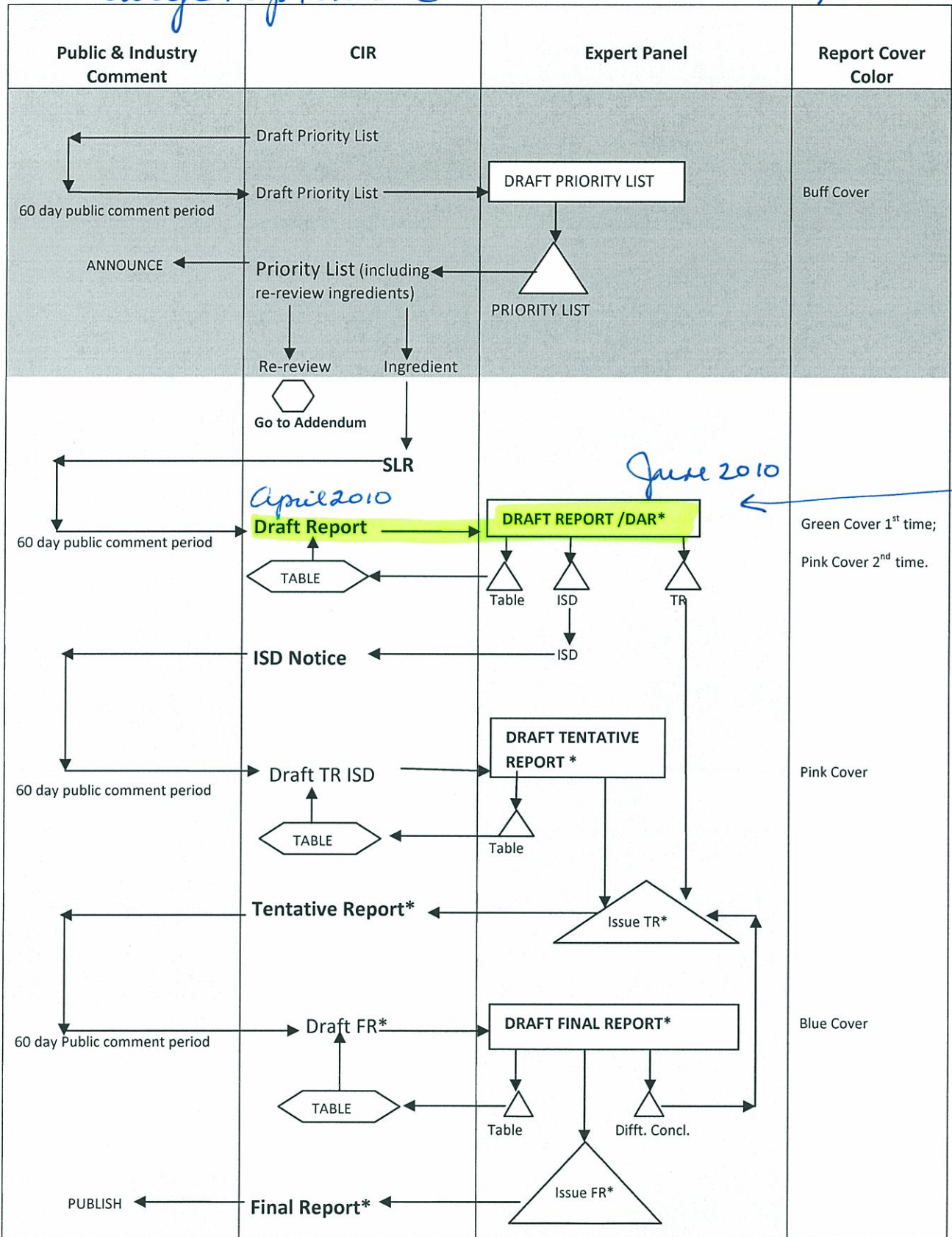
Final Report on the Safety Assessment of Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol

Final Report on the Safety Assessment of Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid

SAFETY ASSESSMENT FLOW CHART

Stearyl Heptanoate

6/2010



*

For ingredient groups originating as Re-Reviews, add word "Amended" before Report; (DAR: Draft Amended Report).



Expert Panel Decision

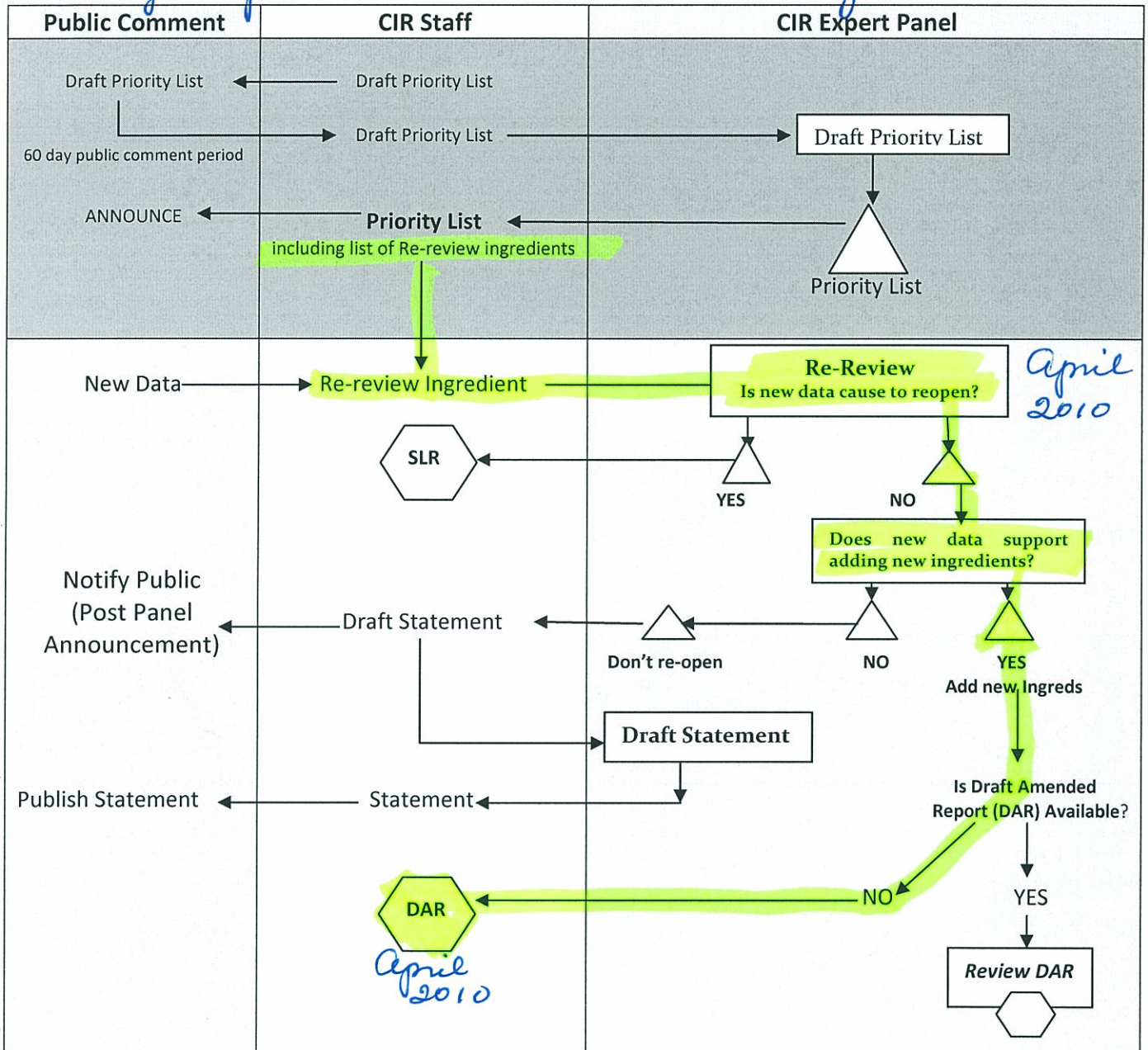


Document for Panel Review

SAFETY ASSESSMENT FLOW CHART: RE-REVIEW ADDENDUM

Sheryl Neptarvate

June 2010



-  CIR Expert Panel Decision Points
-  Document for Panel Review
-  Go To Safety Assessment Flow Chart

CIR Report History for Stearyl Heptanoate

Original Assessment 1995

The Final Report on the Safety Assessment of Stearyl Heptanoate was published in 1994 with the conclusion that Stearyl Heptanoate is “safe for use as a cosmetic ingredient in the present practice of use.”

ReReview: April 4-5, 2010

The rereview was brought before the Expert Panel. While no new safety data were found, additional esters of stearyl alcohol were identified for possible inclusion in the report. The Panel agreed that the existing safety assessment on stearyl heptanoate was sufficient to address the safety of stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate, and stearyl olivate. This review was reopened to include these cosmetic ingredients.

Updated Search – May 3, 2010 – Stearyl Heptanoate Report

TOXNET – limits; citations entered in the last 6 months

Search Strategy:

66009-41-4 OR 18312-31-7 OR 2598-99-4 OR 2778-96-3 OR 24271-12-3 OR (STEARYL AND OLIVATE)

No hits

STN INTERNATIONAL

RTECS

66009-41-4 – 0

18312-31-7 – 0

2598-99-4 – 0

2778-96-3 – 0

24271-12-3 – 0

Stearyl Olivatate – 0

CAPlus

66009-41-4 – 65; mostly patents

18312-31-7 – 57; mostly patents

2598-99-4 – 149; mostly patents

2778-96-3 –

24271-12-3 –

Stearyl Olivatate –

Kosmet

66009-41-4 – 1

18312-31-7 – 0

2598-99-4 – 0

2778-96-3 – 1

24271-12-3 – 0

Stearyl Olivatate – 0

Registry

66009-41-4 – 1

18312-31-7 – 1

2598-99-4 – 1

2778-96-3 – 1

24271-12-3 – 1

Stearyl Olivatate – 0

Merck – 0 hits

WHO – 0 hits

EU – in text

Food additive info – in text

1 PPGs that may be added in the future.

2 DR. BELSITO: Yeah. That's fine.

3 DR. BAILEY: And the conclusion does

4 have the footnote.

5 DR. BELSITO: Yeah. Yeah. And that's

6 fine. Good. Any other comments? Okay. Wow.

7 DR. BRESLAWEK: So your recommendation

8 on this is?

9 DR. BELSITO: Safe as used. It's final.

10 Moving on to tentative final safe as used. Blue

11 book next time.

12 Okay. Another re-review in Buff 2.

13 Stearyl heptanoate. Next to the last tab. Okay.

14 So this safety assessment was published in '95.

15 It was safe as used. There are no new safety

16 data. And search for TOXNET did not find data on

17 any new data. And then search of the dictionary

18 revealed some possible add-ons. Basically stearyl

19 heptanoate is an ester of stearyl alcohol and

20 heptanoic acid. So what other stearyl esters were

21 out there that we haven't reviewed yet? And the

22 answer is there's caprylate, palmitate, stearate,

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1 behenate, and olivate. And again if you searched

2 for those there were no other reports in the

3 literature on them. So the question is if you

4 look at the data that we have, which is when the

5 original report was put in here, do we want to

6 reopen because of new data -- well, there is no

7 new data. Do we want to reopen to add in the

8 other esters? And the question is is there

9 adequate data in the original report to support

10 this?

11 I mean, I thought what we would need and

12 we don't have is the function and the

13 concentration of use for the add-ons. I mean,

14 assuming that the function listed in the

15 dictionary was the same, but then whether we got a

16 concentration of use or not --

17 MS. FIUME: Function is here. On the

18 back of the transmittal.

19 DR. BELSITO: On the back.

20 MS. FIUME: In the very beginning of the

21 very first page of the package. Of the entire

22 report.

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1 DR. BELSITO: Okay.

2 MS. FIUME: Right behind the tab.

3 DR. BELSITO: Ah-ha. Missed it again.

4 MS. FIUME: We're saving paper. A lot

5 of things are backed up.

6 DR. BELSITO: So basically they're skin

7 conditioning agent occlusives and then the

8 concentrations -- updated concentrations of use

9 for stearyl heptanoate are given in the back of

10 the report there. And I thought even though

11 there's very limited data in the report, the

12 original heptanoate report, we could open it for

13 add-ons. We would need the respiratory

14 boilerplate because there would be hairspray.

15 I guess the question -- one question I

16 had is in the -- so the introductory note from

17 Monice. It says the original report for stearyl

18 heptanoate was up to 8 percent, but there's 25

19 percent use in a lip balm in the original report.

20 I thought, unless I was looking at the wrong

21 thing, it says -- it says unpublished data

22 submitted to CIR regarding PCL solid suggests the

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1 mix shall be used in the following concentrations:

2 Lip balms, 5 to 25 percent.

3 MS. FIUME: I was referring to the new

4 information because the 8 percent is the newest

5 information.

6 DR. BELSITO: Oh, okay. I see.

7 MS. FIUME: All went up to 8 percent.

8 DR. BELSITO: Okay. So anyway, that was

9 my open for the add-ons and safe as used, assuming

10 that concentration of use for the add-ons was

11 similar. But any other comments?

12 DR. SNYDER: I agree.

13 DR. LIEBLER: So the main reason to

14 reopen is that there are additional agents that

15 have uses?

16 DR. BELSITO: Yes.

17 DR. LIEBLER: Okay. All right. Because

18 I had said don't reopen because of the apparent

19 lack of additional available data, but I'm

20 learning from you guys still so I'll change my

21 mind.

22 DR. BELSITO: What we're adding on does

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1 have uses, right? I mean, the other ingredients
 2 we're adding on?
 3 MS. FIUME: Yes. The only one that did
 4 not have use --
 5 DR. BELSITO: The olivate a monograph in
 6 development?
 7 MS. FIUME: And stearyl palmitate did
 8 not have any uses according to FDA. Now, the EWG
 9 we looked at to see just -- and that had three.
 10 DR. BELSITO: Right.
 11 MS. FIUME: So it might be zero, but
 12 everything else did have uses.
 13 DR. BELSITO: Okay. So, I mean, add
 14 them on. The number I think we can safely do.
 15 And I think the major question becomes the stearyl
 16 olivate is not currently listed as a cosmetic
 17 ingredient. Is that correct?
 18 MS. FIUME: That's correct.
 19 DR. BELSITO: But there's a monograph
 20 that's in development to add it as a cosmetic
 21 ingredient?
 22 DR. EISENMANN: I haven't looked

1 recently if it's already -- I mean, a lot of these
 2 are done. I mean, they recently updated what's
 3 available online. So we might be able to check
 4 again.
 5 MS. FIUME: And now the only other thing
 6 about that -- Bart's not here -- according to his
 7 map, stearyl olivate is actually, I believe, a
 8 mixture of three -- of three long chains.
 9 DR. EISENMANN: There's probably more
 10 than three, but those are probably the major
 11 chains.
 12 DR. BELSITO: Right. Because it's going
 13 to come from olive oil. Right.
 14 DR. LIEBLER: In that Table 1 with the
 15 new structures, the stearyl palmitate structure is
 16 backwards I think. The chain lengths are
 17 reversed.
 18 MS. FIUME: Table 1.
 19 DR. LIEBLER: I'm sorry, not the table.
 20 SPEAKER: The non-table.
 21 DR. LIEBLER: The first table, right,
 22 the very first table after your memo.

1 DR. BRESLAWEK: For which one?
 2 DR. SNYDER: Right after her memo. On
 3 the back side of her memo.
 4 DR. LIEBLER: Right. The one listed as
 5 stearyl palmitate is incorrect. I think the
 6 chains are swapped. Chain lengths are swapped.
 7 DR. BELSITO: Yeah.
 8 MS. FIUME: So the 17 should be to the
 9 right?
 10 DR. BELSITO: Yeah.
 11 DR. LIEBLER: Right.
 12 DR. KLAASSEN: Well, it's also not the
 13 oxygen there.
 14 DR. LIEBLER: Right. It's listed as a
 15 ketone right now. So.
 16 MS. FIUME: I see what you're talking
 17 about the 25 percent. I had 10.
 18 DR. BELSITO: Okay. So open for
 19 add-ons. Safe as used. And we'll just check on
 20 the stearyl olivate and see what the status is
 21 with that. And then if it's still not yet added
 22 to the dictionary, a little bit in the discussion

1 that it's our assumption that it soon will be
 2 added, that a monograph is in development and
 3 it'll be added and used similar to the other
 4 ingredients in this report.
 5 Okay, disperse Blue 1. And this is also
 6 a re-review. So the safety assessment in this was
 7 published in '95 with it a safe up to 1 percent.
 8 The basis for the 1 percent limit was not clear.
 9 There's no new data except that it's been
 10 considered by IARC and they now seem to be coming
 11 down on the side of possibly carcinogenic in
 12 humans. Certainly, when we looked at this in '95,
 13 we looked at carcinogenicity data very strongly
 14 and that's in our discussion. It should be noted
 15 that this is banned in Europe. Is that correct?
 16 And banned because of their concerns about
 17 carcinogenicity. We now know that it's not being
 18 used in the United States anymore. Is that
 19 correct?
 20 DR. EISENMANN: As far as we're aware
 21 of.
 22 DR. BELSITO: So the question is do we

1 DR. MARKS: I'm not sure, as long as
2 it's safe -- that we're going to resolve -- but
3 you're exactly right, Ron. When you look at it,
4 there's a discrepancy between the minutes and the
5 final report.

6 Okay. Since we won't be able to roll
7 back time, we'll move on, then, to stearyl
8 heptanoate. And that's a re-review in Buff 2.
9 Next tab back.

10 So, in '95, the -- it was concluded that
11 stearyl heptanoate is safe for use and now there's
12 no new data and no relevant public literature was
13 found, but we have five ingredients if you look at
14 the memo from -- and these five ingredients that
15 we possibly could add on.

16 So the question is, do we reopen for
17 these add ons, these fatty esters, and are they
18 simple? And is it a no-brainer?

19 The two Rons.

20 DR. SHANK: Reopen the document to add
21 those ingredients.

22 DR. HILL: I agree with that. But I

1 wondered if it was possible to wait on the elevate
2 -- monograph, since it was being worked on.

3 MS. FIUME: It may be available at this
4 time. We'll double check tonight. Carol seems to
5 think it might be. So, we're going to check on
6 that.

7 DR. HILL: I know tabling is sort of a
8 last resort option, but I wonder if we know that
9 monograph is coming and I agree with him,
10 reopening should be, in this case, a very good
11 idea.

12 DR. ANDERSEN: Yeah, I think it will
13 catch up with what we're doing --

14 DR. HILL: Okay.

15 DR. ANDERSEN: -- and the two can hit
16 you at the same time.

17 DR. MARKS: Okay. So we'll reopen this
18 and a SLR will be issued, correct?

19 DR. ANDERSEN: No.

20 DR. MARKS: No, we open it with a
21 tentative --

22 DR. ANDERSEN: We're going to -- what we

1 will present to you at the next meeting is a draft
2 tentative amended --

3 DR. MARKS: Amended.

4 DR. ANDERSEN: -- safety assessment that
5 will simply add these, will include the new
6 monograph for the olivate, and allow you to make
7 the decision that that all looks good to you and
8 issue it as a tentative amended.

9 DR. MARKS: So, again and procedurally,
10 essentially will you be sending out a notice and
11 will it be actually an SLR, Scientific Literature
12 Request, or not?

13 DR. ANDERSEN: No, we'll -- industry by
14 the fact that we're reopening it to add the
15 ingredients, is on the alert that there is an
16 opportunity to submit unpublished data. We're not
17 asking for any particularly, but if there are
18 unpublished data, now would be the time to submit
19 them. Those can be incorporated into the draft
20 that the panel will review ostensibly in June.

21 So, no. We're not going back to square
22 1. We're going to keep proceeding apace to make

1 no ingredients that were identified as possible
2 add-ons. There were only two cases in the
3 literature of allergic contact dermatitis to
4 quaternium-22. Our team felt that we did not need
5 to reopen this so we moved not to reopen.

6 DR. BELSITO: Second.

7 DR. BERGFELD: Second. Is there any
8 further discussion about this particular
9 ingredient? Seeing none I call for the question,
10 all those in favor of not reopening? Unanimous.
11 Thank you.

12 Moving on to the last ingredient that's
13 in this re-review group is stearyl heptanoate.
14 Dr. Belsito?

15 DR. BELSITO: This is stearyl
16 heptanoate, and in 1995 we looked at it, safe as
17 used. Since that time there has been no
18 significant new safety data. The types of
19 products and concentrations of use have remained
20 relatively stable. However, stearyl heptanoate is
21 an ester of stearyl alcohol and heptanoic acid and
22 there are a number of other esters of syearyl

1 alcohol that we might want to include,
2 particularly stearyl caprylate, palmitate,
3 stearate, behenate, and olivate, and we felt that
4 we should go to reopen these to add in those
5 esters.

6 DR. BERGFELD: That's a motion?

7 DR. BELSITO: That is a motion.

8 DR. BERGFELD: Is there a second?

9 DR. MARKS: Second.

10 DR. BERGFELD: Is there any further
11 discussion about reopening this ingredient?

12 Seeing none I call for the question, all those in
13 favor indicate by raising your hand. Thank you.
14 Unanimous.

15 Now we're on to the re-review summaries
16 and Dr. Andersen is going to discuss these.

17 DR. ANDERSEN: What we're searching for
18 is our ongoing effort to capture in as best a way
19 possible the panel's decisions to not reopen
20 re-reviewed safety assessments. We have two
21 decisions to not reopen from the December meeting
22 and the idea is that we would like your feedback

**Draft Amended Report of the Cosmetic Ingredient Review
Expert Panel**

**on the Safety Assessment of Stearyl Heptanoate and Related
Stearyl Alkanoates as Used in Cosmetics**

June 28-29, 2010

The 2010 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D; Curtis D. Klaassen, Ph.D.; Daniel Liebler, Ph.D; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This report was prepared by Monice M. Fiume, CIR Scientific Analyst/Writer.

Cosmetic Ingredient Review

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ABSTRACT

Stearyl heptanoate is a stearyl alkanoate (the ester of stearyl alcohol and heptanoic acid) that functions in cosmetics as a skin conditioning agent. Stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate, and stearyl olivate are also stearyl alkanoates with similar structures and similar functions. The safety information included in this review applies to stearyl heptanoate or some of the components of these alkanoates. The Panel determined that the available information could support the safety of all of the related stearyl alkanoates. No toxicological concerns were raised by any of this information. Genotoxicity and carcinogenicity testing was negative. The ingredients were not dermal irritants and did not appear to be sensitizers or ocular irritants. The Expert Panel concluded that stearyl heptanoate, stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate, and stearyl olivate are safe in the present practices of use and concentration.

INTRODUCTION

Stearyl Heptanoate has previously been reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel. In 1995, the safety assessment was published with the conclusion that stearyl heptanoate is “safe for use as a cosmetic ingredient in the present practice of use.”¹ Recently, a search of the published literature found no new published studies. This was not surprising since the data in the original safety assessment was almost exclusively unpublished. Therefore, there was no reason to reassess the safety of stearyl heptanoate based on new information.

However, additional stearyl alkanoates are used as cosmetic ingredients. The Expert Panel determined that the safety data included in the 1995 assessment of stearyl heptanoate are applicable to the safety of stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate, and stearyl olivate. Accordingly, these ingredients will be included in this review.

This report is an update of the 1995 safety assessment, and as such, it would normally contain only information available after the 1995 assessment was issued. However, the new information was limited primarily to use data. *A brief summary of information from the original safety assessment is included in italics for the absorption, toxicology and clinical sections.* Even at the time of the 1995 assessment, limited data were available on stearyl heptanoate itself. Since stearyl alkanoates are metabolized by esterases in the body to stearyl alcohol and the related fatty acid,²⁻⁴ relevant data from the report on stearyl alcohol were included to support safety. As such, *a brief summary of relevant information from the stearyl alcohol report⁵ will also be included in italics.* (It was concluded that stearyl alcohol was safe as used in cosmetics. Stearyl alcohol was used at concentrations $\leq 50\%$.)

A CIR safety assessment is available for palmitic acid and stearic acids,⁶ the fatty acid components of stearyl palmitate and stearyl stearate, respectively. So as was done in the 1995 assessment on stearyl heptanoate, *summaries from the report on these components will be included in this report as well, and this information will also be in italics.* (It was concluded that palmitic and stearic acid were safe as used in cosmetics. Palmitic acid was used at concentrations $\leq 25\%$ and stearic acid was used at concentrations $> 50\%$.)

CHEMISTRY

Definition and Structure

The definition, synonyms, and function in cosmetics for stearyl heptanoate, stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate,⁷ and stearyl olivate⁸ are given in Table 1. The structure map of these chemicals is given in Figure 1.

USE

Cosmetic

All of the stearyl alkanoates included in this report function as skin conditioning agents.⁷ Some have additional uses. (See Table 1). According to information supplied to the Food and Drug Administration (FDA) as part of the Voluntary

Cosmetic Registration Program (VCRP), at the time of the original assessment, Stearyl Heptanoate was used in 121 cosmetic formulations in 1994.¹ Concentration of use was not reported to FDA at the time of the original safety assessment, but unpublished data reported use at up to 25%. Since then, frequency as well as concentration of use has decreased. Recent VCRP data indicate that stearyl heptanoate is used in 102 cosmetic formulations.⁹ Results of a survey of current use concentrations conducted by the Personal Care Products Council (Council) indicate that stearyl heptanoate is now used at concentrations of 0.07-8%.¹⁰ Current and historical use data are given in Table 2.

According to VCRP data, stearyl caprylate, stearyl stearate, and stearyl olivate are used in cosmetics, and the frequency of use of these ingredients is 20, 22, and 1, respectively.⁹ According to the results of a concentration of use survey conducted by the Council, stearyl caprylate is used at concentrations of 0.1-1% and stearyl stearate is used at concentrations of 0.02-4%.¹¹ No uses were reported for stearyl olivate in response to the survey. Stearyl palmitate and stearyl behenate are not reported to be used according to VCRP data.⁹ However, according to the survey of use concentrations conducted by the Council, stearyl palmitate and stearyl behenate are used in formulations applied to the eye at concentration of 3% and 0.02%, respectively.¹¹ (See Table 2 for use details).

Stearyl heptanoate and stearyl stearate are used in products that may be inhaled, and effects on the lungs that may be induced by inhaled products containing these ingredients are of concern.

The aerosol properties that determine deposition in the respiratory system are particle size and density. The parameter most closely associated with deposition is the aerodynamic diameter, d_a , defined as the diameter of a sphere of unit density possessing the same terminal settling velocity as the particle in question. In humans, particles with an aerodynamic diameter of $\leq 10\mu\text{m}$ are respirable. Particles with a d_a from 0.1 - $10\mu\text{m}$ settle in the upper respiratory tract and particles with a $d_a < 0.1 \mu\text{m}$ settle in the lower respiratory tract.^{12,13}

Particle diameters of 60-80 μm and $\geq 80 \mu\text{m}$ have been reported for anhydrous hair sprays and pump hairsprays, respectively.¹⁴ In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 μm range and the mean particle diameter in a typical aerosol spray has been reported as $\sim 38 \mu\text{m}$.¹⁵ Therefore, most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

Internationally, there are no restrictions on the use of stearyl heptanoate, stearyl caprylate, stearyl palmitate, stearyl stearate, or stearyl behenate in the European Union.¹⁶ Stearyl olivate is not listed by the European Union.

Non-Cosmetic

Stearyl palmitate and stearyl stearate are included on the list of indirect additives used in food contact substances.¹⁷

GENERAL BIOLOGY

Absorption, Distribution, Metabolism, and Excretion

Stearyl alcohol is found naturally in various mammalian tissues and is readily converted to stearic acid.⁵ Stearyl alcohol is poorly absorbed from the gastrointestinal tract. Fatty acids are absorbed, digested, and transported in animals and humans.⁶ Palmitic and stearic acids are primarily transported via the lymphatic system. In digestion studies, stearic acid was the most poorly absorbed of the common fatty acids.

ANIMAL TOXICOLOGY

Acute Toxicity

The oral LD_{50} of stearyl heptanoate, concentration not specified, was $>16 \text{ ml/kg}$ for albino Sprague-Dawley rats.¹ A cosmetic formulation containing 0.7% stearyl heptanoate given orally to Sprague Dawley rats had an $LD_{50} >5.0 \text{ g/kg}$. The LD_{50} of stearyl alcohol was $>8 \text{ g/kg}$ when given orally to Holtzman albino rats.⁵ The oral LD_{50} of palmitic acid was $>10 \text{ g/kg}$ for rats, and 5 g/kg a shaving cream containing 2.2% palmitic acid given orally and dermally was non-toxic.⁶ The

oral LD₅₀s of cosmetic formulations containing ≤13% stearic acid were >5g/kg for rats. Mild erythema and slight induration of skin was observed in an acute study with rabbits and guinea pigs dosed with ≤100 mM stearic acid.

Short-Term Toxicity

No toxic effects were observed when chicks were fed diets containing 50% stearic acid for 4 wks.⁶ Application of 18 mmol% palmitic acid to the external ear canal of rabbits for 6 wks caused slight irritation for the first 2 wks. In a 4-wk study, application of a formulation containing 20% stearic acid to abraded and intact skin of rabbits produced slight edema and desquamation, but it did not raise any toxicologic concerns.

Subchronic Toxicity

No evidence of systemic toxicity was observed with a formulation containing 8.0% stearyl alcohol in a 3-month percutaneous study using rabbits.⁵ In 13-wk dermal toxicity studies, application of formulations containing ≤5% stearic acid produced minimal to mild irritant effects.⁶

Dermal Irritation

Undiluted stearyl heptanoate was mildly irritating to rabbit skin.¹ Undiluted stearyl alcohol applied under occlusion was minimally to mildly irritating to rabbit skin.⁵ Palmitic acid, as supplied and in formulation at ≤74%, and stearic acid, as supplied and in formulation at ≤65%, were at most mildly irritating.⁶

Sensitization

A cosmetic formulation containing 1.5% stearyl heptanoate was not a sensitizer using guinea pigs.¹ A deodorant formulation containing 24.0% stearyl alcohol was not a contact sensitizer.⁵ A formulation containing 1% stearic acid was a weak, grade 1, sensitizer using guinea pigs, while in a maximization study, a cosmetic formulation containing 3.5% stearic acid was not a sensitizer.⁶

Photosensitization

Cosmetic formulations containing 2.8% stearic acid were not phototoxic or photoallergenic.⁶

Comedogenicity

A cosmetic formulation containing 1.5% stearyl heptanoate produced slight to moderate comedogenicity in rabbit ears.¹ Stearyl alcohol was not comedogenic when applied to the ear canal of rabbits.⁵

Ocular Irritation

Undiluted stearyl heptanoate was classified as a category 3 (not defined) eye irritant using rabbits. Cosmetic formulations containing 0.7 or 1.5% stearyl heptanoate were not primary eye irritants.¹ Undiluted stearyl alcohol was minimally irritating to rabbit eyes.⁵ Palmitic acid, as supplied and in formulations at ≤19.4%, produced at most mild irritation, but were generally non-irritating to rabbit eyes.⁶ Stearic acid, as supplied and in formulation at ≤65%, produced some initial mild ocular irritation.

GENOTOXICITY

A mixture containing >50% stearyl heptanoate, at ≤5000 µg/plate, did not induce base pair or frameshift mutations with or without metabolic activation.¹ The mixture, ≤5000 mg/kg, did not have a clastogenic effect in a micronucleus test. Stearyl alcohol, concentration tested not given, was not mutagenic in an Ames assay with or without metabolic activation.⁵ Stearic acid, 50 µg/plate, was not mutagenic in an Ames assay, and ≤500 µg/ml did not induce mitotic aneuploidy.

CARCINOGENICITY

Palmitic and stearic acids were not carcinogenic to mice given ≤5.0 or ≤1.0 mg injections, respectively, 2-3 times per wk for a total of ≤26 injections.⁶

Tumor Promotion

Stearyl alcohol did not promote tumor formation in female Swiss mice when initiated with 7,12-dimethylbenz[a]-anthracene.⁵

CLINICAL ASSESSMENT OF SAFETY

Irritation and Sensitization

Stearyl heptanoate, tested at an unspecified concentration and in formulations containing $\leq 1.5\%$, was not an irritant or sensitizer, and daily patch testing of formulations containing 8-24% stearyl heptanoate was essentially non- to slightly irritating.¹ Undiluted stearyl alcohol was a mild irritant in a single insult occlusive patch test.⁵ Four of 1664 subjects had an allergic reaction to 30% stearyl alcohol in liquid paraffin. Cosmetic formulations containing 2.2% palmitic acid were non-irritating and non-sensitizing.⁶ Formulations containing $\leq 40\%$ stearic acid were generally non-irritating, except for on formulation containing 2.8% stearic acid, which was moderately irritating in a 21-day cumulative irritation assay. In sensitization assays, $\leq 13\%$ stearic acid in cosmetic formulations produced some irritation at induction, but generally no reaction at challenge.

Photosensitization

A cosmetic formulation containing 2.2% palmitic acid was non-photosensitizing and cosmetic formulations containing $\leq 23\%$ stearic acid were not phototoxic, photosensitizing, or photoallergenic.⁶

Comedogenicity

A cosmetic formulation containing 1.5% stearyl heptanoate was not comedogenic.¹

SUMMARY

Stearyl heptanoate has previously been reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel, and, in 1995, it was concluded that this ingredient was safe as used. A recent search of the literature published since that report was issued did not find any new data. However, the Panel agreed that stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate, and stearyl olivate were similar to stearyl heptanoate, and that the original safety assessment on stearyl heptanoate could address the safety of these stearyl alkanooates as well. Therefore, a rereview was initiated to include these ingredients.

The stearyl alkanooates reviewed in this safety assessment all function as skin conditioning agents; some have a few other functions. In 1994, it was reported to the Food and Drug Administration (FDA) that stearyl heptanoate was used in 121 cosmetic formulations, and, according to unpublished data, it was being used at up to 25%. As of 2010, the frequency of use has decreased to 102, and, according to an industry survey, use concentrations have decreased and are now $\leq 8\%$. It has been reported to the FDA that stearyl caprylate, stearyl stearate, and stearyl olivate are used in 20, 22, and 1 cosmetic formulations, respectively. According to an industry survey, stearyl caprylate is used at concentrations of 0.1-1%, stearyl stearate is used at 0.02-4%, and stearyl olivate is not reported to be used. Stearyl palmitate and stearyl behenate are not reported to be in use according to VCRP data, however, industry data reports that these ingredients are used in eye products at concentrations of 3 and 0.02% respectively.

Since published data were not found for these ingredients, summaries from the original safety assessment on stearyl heptanoate and from available CIR assessments on some of the components of these stearyl alkanooates, i.e. stearyl alcohol, palmitic acid, and stearic acid, were included in this review. The information from these previous assessments did not raise any toxicological concerns, and there were no concerns of genotoxic effects. Also, these ingredients were at most mildly irritating to the skin, and they did not appear to be sensitizers. Palmitic acid and stearic acid were not phototoxic. Stearyl heptanoate produced slight to moderate comedogenicity in rabbit ears, but was not comedogenic for humans. At most, mild ocular irritation was seen in testing with any of these ingredients.

DRAFT DISCUSSION

The CIR Expert Panel initiated a rereview of stearyl heptanoate to include stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate, and stearyl olivate. While published data were not available for these ingredients, the Expert Panel determined that these stearyl alkanoates were similar to stearyl heptanoate, and that the original safety assessment on stearyl heptanoate could address these ingredients as well. In the original safety assessment on stearyl heptanoate, the Panel noted that although animal irritation testing was done at 100%, sensitization testing was performed using a maximum concentration of only 1.5% stearyl heptanoate. The Panel agreed then, and agrees now, that all the available data suggest that stearyl heptanoate would not be a sensitizer, even at higher concentrations. The same would apply to the stearyl alkanoates now included in this rereview. In the original safety assessment, it was also noted that mild ocular reactions were seen in ocular irritation testing with undiluted stearyl heptanoate. The Panel is still of the opinion that stearyl heptanoate, as used in cosmetic formulations, would not produce significant ocular irritation. The same is true for the related stearyl alkanoates.

Stearyl heptanoate and stearyl stearate are used in cosmetic formulations that can be inhaled. The potential adverse effects of inhaled ingredients depend on the specific chemical species, the concentration and the duration of the exposure and their site of deposition within the respiratory system. In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 μm range and the mean particle diameter in a typical aerosol spray has been reported as $\sim 38 \mu\text{m}$. Particles with an aerodynamic diameter of $\leq 10\mu\text{m}$ are respirable. In the absence of inhalation toxicity data, the panel determined that stearyl heptanoate and stearyl stearate can be used safely in products that are inhaled, because the product particle size is not respirable.

DRAFT CONCLUSION

The CIR Expert Panel concluded that stearyl heptanoate, stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate, and stearyl olivate are safe in the present practices of use and concentration.¹

¹ Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

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Figure 1. Figure map of stearyl alkanoates.

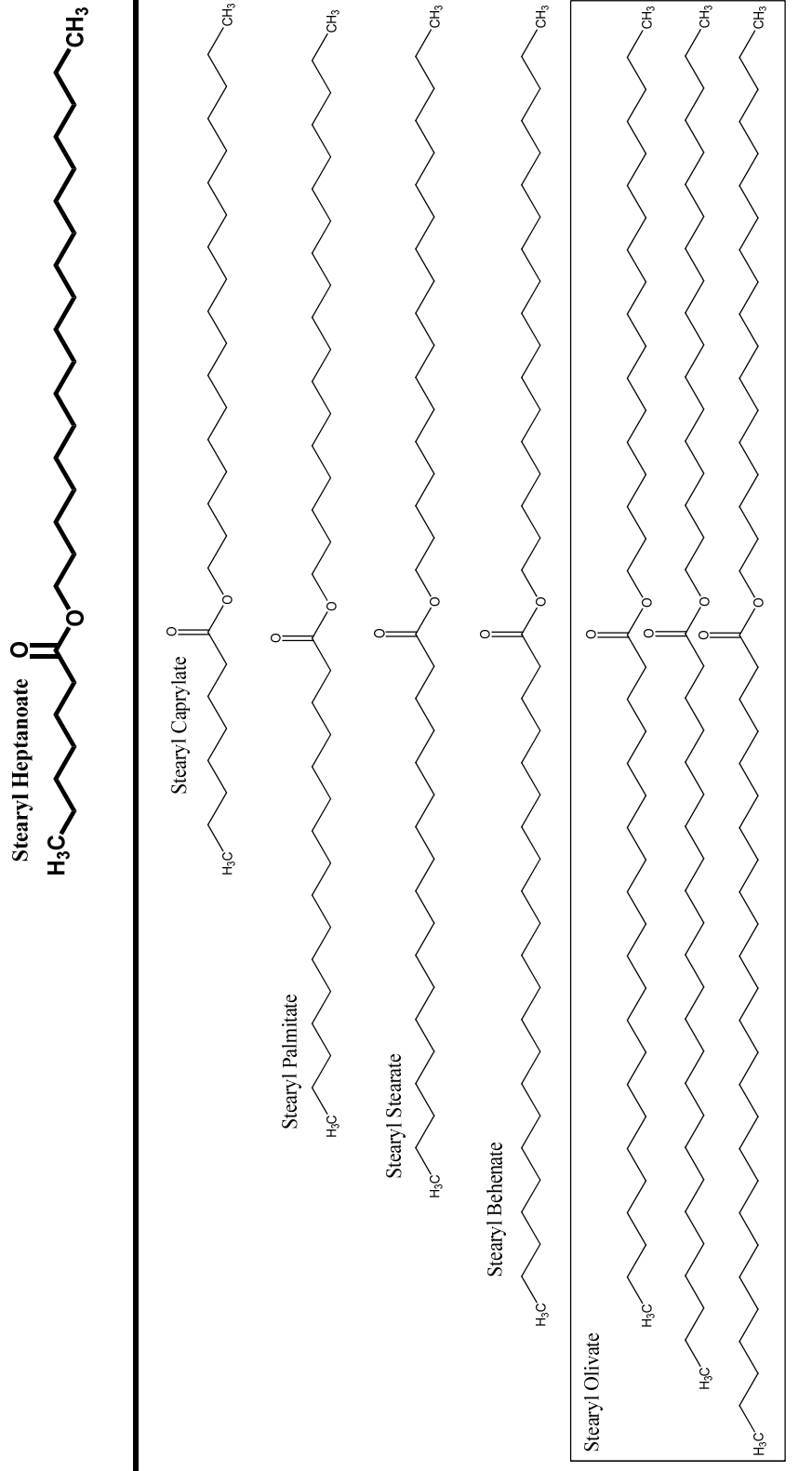


Table 1. Definitions, synonyms, and cosmetic functions.

INGREDIENT (CAS No.)	DEFINITION	SYNONYMS	COSMETIC FUNCTION
Stearyl Heptanoate (66009-41-4)	the ester of stearyl alcohol and heptanoic acid	heptanoic acid, octadecyl ester	skin conditioning agent – occlusive
Stearyl Caprylate (18312-31-7)	the ester of stearyl alcohol and caprylic acid	octanoic acid, octadecyl ester	skin conditioning agent – occlusive
Stearyl Palmitate (2598-99-4)	the ester of stearyl alcohol and palmitic acid (q.v.)	hexadecanoic acid, octadecyl ester	binder; emulsion stabilizer; hair conditioning agent; humectant; opacifying agent; skin conditioning agent - miscellaneous
Stearyl Stearate (2778-96-3)	the ester of stearyl alcohol and stearic acid	octadecanoic acid, octadecyl ester	skin conditioning agent – occlusive; viscosity increasing agent - nonaqueous
Stearyl Behenate (24271-12-3)	the ester of stearyl alcohol (q.v.) and behenic acid (q.v.)	docosanoic acid, octadecyl ester	skin conditioning agent – occlusive
Stearyl Oliviate (no CAS No.)	the ester of stearyl alcohol and the fatty acids derived from Olea europaea (olive) oil (q.v.); olive oil is composed of a number of fatty acids, primarily oleic, linoleic, palmitic, palmitoleic, and stearic acids		skin conditioning agent; emollient; surfactant – emulsifying agent

Table 2. Frequency of use according to duration and exposure.

Total # Uses/ Category (2009)	Stearyl Heptanoate					
	1994		1993*		2010	
	Freq. of Use	Freq. of Use	Conc of Use (%)	Conc of Use (%)	Freq. of Use	Conc of Use (%)
TOTAL	121	102	2-25	2-25	0.07-8	0.07-8
Leave-On	20,939	99	2-25	2-25	0.07-8	0.07-8
Rinse Off	13,453	3	NR	NR	0.7-3	0.7-3
Eye	3359	17	NR	NR	0.5-8	0.5-8
Possible Ingestion	2102	8	5-25	5-25	3-8	3-8
Inhalation	3208	2	NR	NR	0.7	0.7
Dermal	24919	100	2-25	2-25	0.07-8	0.07-8
Hair - Non-Coloring	5298	4	NR	NR	NR	NR
Hair - Coloring	2839	0	NR	NR	NR	NR
Nail	617	0	NR	NR	NR	NR
Mucous Membrane	3430	0	NR	NR	NR	NR
Deodorant (underarm)	580	0	NR	NR	0.07	0.07
Baby Products	336	0	NR	NR	NR	NR

Total # Uses/ Category (2009)	Stearyl Caprylate		Stearyl Palmitate		Stearyl Stearate		Stearyl Behenate		Stearyl Oliviate	
	2010		2010		2010		2010		2010	
	Freq. of Use	Conc. of Use (%)	Freq. of Use	Conc. of Use (%)	Freq. of Use	Conc. of Use (%)	Freq. of Use	Conc. of Use (%)	Freq. of Use	Conc. of Use (%)
TOTAL	20	0.1-1	0	3	22	0.02-4	0	0.02	1	NR
Leave-On	19	0.3-1	0	3	20	0.02-4	0	0.02	0	NR
Rinse Off	1	0.1-0.6	0	0	2	2	0	NR	1	NR
Eye	2	≤1	0	3	5	≤1	0	0.02	0	NR
Possible Ingestion	2	NR	0	0	5	≤1	0	NR	0	NR
Inhalation	0	NR	0	0	1	NR	0	NR	0	NR
Dermal	20	≤1	0	0	16	4≤	0	NR	1	NR
Hair - Non-Coloring	0	NR	0	0	1	3	0	NR	0	NR
Hair - Coloring	0	NR	0	0	0	NR	0	NR	0	NR
Nail	0	NR	0	0	0	NR	0	NR	0	NR
Mucous Membrane	1	NR	0	0	2	2	0	NR	0	NR
Deodorant (underarm)	0	NR	0	0	0	NR	0	NR	0	NR
Baby Products	0	NR	0	0	0	NR	0	NR	0	NR

NR - no use reported by industry for this category

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: John Bailey, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: May 13, 2010

SUBJECT: Concentration of Use Additions to the Stearyl Heptanoate report
Stearyl Caprylate, Stearyl Palmitate, Stearyl Stearate, Stearyl Behenate and Stearyl Olivat

**Concentration of Use - Additions to the Stearyl Heptanoate Report
 Stearyl Caprylate, Stearyl Palmitate, Stearyl Stearate, Stearyl Behenate, Stearyl Olivat***

Ingredient	Product Category	Concentration of Use
Stearyl Caprylate	Eyeliners	0.3%
Stearyl Caprylate	Eye lotion	1%
Stearyl Caprylate	Foundations	0.7-0.8%
Stearyl Caprylate	Other makeup preparations	0.7%
Stearyl Caprylate	Shaving cream (aerosol, brushless and lather)	0.6%
Stearyl Caprylate	Body and hand creams, lotions and powders	0.6-0.9%
Stearyl Caprylate	Paste masks (mud packs)	0.1%
Stearyl Palmitate	Mascara	3%
Stearyl Stearate	Mascara	0.2-1%
Stearyl Stearate	Tonics, dressings and other hair grooming aids	3%
Stearyl Stearate	Foundations	0.8-4%
Stearyl Stearate	Lipstick	0.4-1%
Stearyl Stearate	Bath soaps and detergents	2%
Stearyl Stearate	Body and hand creams, lotions and powders	0.02%
Stearyl Stearate	Other skin care preparations	2%
Stearyl Behenate	Mascara	0.02%

*Ingredients included in the title of the table but not found in the table were included in the survey, but no uses were reported.

Information collected in 2010
 Table prepared May 12, 2010