NOSB COMMITTEE RECOMMENDATION

Form NOPLIST1. Committee Transmittal to NOSB

For NOSB Meeting: __Fall 2011	Substance: _ Arachidonic acid single-cell oil (ARA)

Committee: Crops • Livestock • Handling X Petition is for:__Inclusion on the National List 7CFR § 205.605(a)

A. Evaluation Criteria (Applicability noted for each category; Documentation attached) **Criteria Satisfied? (see B below)**

1. Impact on Humans and Environment — Yes X No • N/A •
2. Essential & Availability Criteria — Yes X No • N/A •
3. Compatibility & Consistency — Yes X No • N/A •
4. Commercial Supply is Fragile or Potentially Unavailable as Organic (only for 606) — Yes • No • N/A X

B. Substance Fails Criteria Category: _____ Comments: _____

_____

C. Proposed Annotation (if any): _____

_____

Basis for annotation: To meet criteria above: _____ Other regulatory criteria: _____ Citation:_____

D. Recommended Committee Action & Vote (State Actual Motion): ____Approve as

Motion is list the material as a non-synthetic, designating the material for §205.605(a)

Motion by: _Tracy MIedema_____ Seconded:_Steve DeMuri_____ Yes: 6_____ No: _0____ Absent: __1_____ Abstain: ___0__

Motion is to list the petitioned material Arachidonic acid single-cell oil (ARA) on the National List 7 CFR, §205.605(a) as Arachidonic acid single-cell oil (ARA)

Motion by: _Tracy Miedema_____ Seconded:___Steve DeMuri_____ Yes: ___6__ No: __0___ Absent: __1_____ Abstain: __0___

Crops		Agricultural		Allowed[1]	X
Livestock		Non-Synthetic	X	Prohibited[2]	
Handling	X	Synthetic		Rejected[3]	
No restriction		Commercially Un-Available as Organic[1]		Deferred[4]	

1) Substance voted to be added as "allowed" on National List to § 205._____with Annotation (if any) _____

_____

2) Substance to be added as "prohibited" on National List to § 205._____with Annotation (if any) _____

_____

Describe why a prohibited substance:_____

_____

3) Substance was rejected by vote for amending National List to § 205. _____Describe why material was rejected:_____

_____

4) Substance was recommended to be deferred because _____

_____ If follow-up needed, who will follow up _____

E. Approved by Committee Chair to transmit to NOSB:

Steve DeMuri_____ **October 7, 2011**

Committee Chair **Date**

NOSB EVALUATION CRITERIA FOR SUBSTANCES ADDED TO THE NATIONAL LIST

Category 1. Adverse impacts on humans or the environment? **Substance** **Arachidonic acid single-cell oil (ARA)**

Question	Yes	No	N/A[1]	Documentation (TAP; petition; regulatory agency; other)
1. Are there adverse effects on environment from manufacture, use, or disposal?[1] [§205.600 b.2]		x		The TR concluded that the petitioned substance, ARA Single-cell Oil, is produced primarily by a "non-genetically-modified soil fungus *Mortierella alpina*," and that the fungus is safe for consumption by humans and other life. *See TR at lines* 204-205 (fungus "not believed to cause disease in humans and biota.") The TR described the production, extraction and purification method of the natural oil. *See TR lines 212-256.* The TR noted that the post-extraction and purification processes "remove any extraction and purification solvents from the oil," *see TR at lines 270-73,* and concluded that the removed solvents are typically "recycled and reused." *See TR at 271-2* Any other impurities such as "trace metals, and oxidation products" are "removed physically through filtration or addition of adsorbents" *See TR at lines 249-50* Lastly, the *TR* stated at *273*: "No residual hexane from the extraction process has been detected in samples of ARA Single-cell Oil using methods with detection limits of 0.3 ppm ." The TR also cited a single Swiss study that tested more than 40 non-organic vegetable oils that used a similar extraction technology for hexane residues and concluded that less than 13% had any detectable residue and the level was "below acceptable tolerances." *See TR at line 237* *See also Question 2 below*
2. Is there environmental contamination during manufacture, use, misuse, or disposal? [§6518 (m)(3)]		x		The TR concluded that the petitioned substance is produced under completely controlled conditions--"aerobic fermentation of the fungus in shake flasks containing a growth medium." *See generally TR line212; see also generally TR lines 204-256* (describing inputs, manufacturing process and waste byproducts) Because the fungus is grown in a controlled environment, there appear to be no environmental issues arising from the process. *see also lines* 407-409 (noting FDA GRAS notice reported no heavy metals or pesticides detected in petitioned substance)
3. Is the substance harmful to the environment? [§6517c(1)(A)(i);6517(c)(2)(A)i]		x		*See* Question 2 above, citing *TR lines* 204-256; *see also TR at lines* 204-205 (fungus "not believed to cause disease in humans and biota.")
4. Does the substance contain List 1, 2, or 3 inerts? [§6517 c (1)(B)(ii); 205.601(m)2]			x	This is a substance used as an ingredient in an organic processed food. It is not used in production and contains no listed inerts.

[1]The criteria set forth in 7 CFR §205.600(b) are applicable solely to "synthetic substances used as a processing aid or adjuvant." The petitioned substance is not a processing aid or adjuvant. *See TR at line 90-94* The TR determined the petitioned substance be a non-synthetic. *See TR at line 286* ("ARA Single-cell Oil does not appear to be a synthetic substance.") Accordingly, the criteria listed in §205.600(b) are inapplicable to the petitioned substance. *See e.g.* 7 CFR §205.600(c)("Non-synthetics…will be evaluated using the criteria [in the OFPA].") However, the TR included review of most of these questions so the results are cited out of an abundance of caution.

5. Is there potential for detrimental chemical interaction with other materials used? [§6518 m.1]			x	The substance is used as an ingredient in an organic processed food. No detrimental interactions were noted in the TR. *See TR lines 123-145* (discussing combinations with substances in formulations); *see also TR at lines* 204-205 (fungus "not believed to cause disease in humans and biota.")
6. Are there adverse biological and chemical interactions in agro-ecosystem? [§6518 m.5]			x	This is a substance used as an ingredient in an organic processed food. It is no longer in the agro-ecosystem. *See also TR at lines* 204-205 (fungus "not believed to cause disease in humans and biota.")
7. Are there detrimental physiological effects on soil organisms, crops, or livestock? [§6518 m.5]			x	This is a substance used as an ingredient in an organic processed food. It is no longer in the agro-ecosystem. *See also TR at lines* 204-205 (fungus "not believed to cause disease in humans and biota.")
8. Is there a toxic or other adverse action of the material or its breakdown products? [§6518 m.2]			x	This is a substance used as an ingredient in an organic processed food. It is no longer in the agro-ecosystem. *See also TR at lines* 204-205 (fungus "not believed to cause disease in humans and biota.")
9. Is there undesirable persistence or concentration of the material or breakdown products in environment?[§6518 m.2]			x	This is a substance used as an ingredient in an organic processed food. It is no longer in the agro-ecosystem. *See also TR at lines* 204-205 (fungus "not believed to cause disease in humans and biota.")
10. Is there any harmful effect on human health? [§6517 c (1)(A)(i) ; 6517 c(2)(A)i; §6518 m.4]		x		**The Safety of the Fungus:** The TR concluded that the scientific literature regarding the fungus from which the oil is extracted discloses that there is no reason to believe that any harm to humans or other life will occur. *See TR at lines* 204-205 **Health Benefits from Consumption:** With regard to the health of those that consume the petitioned substance, the TR concluded: "Research suggests that a balance of ARA and DHA are necessary to the normal growth and development of infants." *See TR at lines 126-27* The TR also noted that many studies have reported "statistically significant improvements to retinal maturation, visual acuity, and cognitive function" while one study cited "reported no benefit." *See TR at lines 418-32* The TR appears to conclude the vast body of evidence of health benefits far outweighed the single study that found no measurable benefit. The TR also cited the World Health Organization ("WHO") recommendation that "ARA should be supplied in the diets of infants aged 0–6 months" and noted the Institute of Medicine has established intake levels for infants aged 0–6 months and small children. See TR at lines, 593-596 **Safety Analysis** "ARA Single-cell Oil is generally recognized as safe for human consumption, even in vulnerable infant populations." *See TR at lines, 496-97* The TR cited the "most recent safety assessment of ARA Single-cell Oil" in the scientific literature, *TR at lines 448-52*, and summarized its findings: "All results of the genotoxicity assays were negative" and "No adverse effects attributed to consumption of the ARA Single-cell Oil were observed even at the highest dose" which in the study was "29-times higher than the anticipated intake" for term infants. *See also TR at lines 459-62* (noting that Australia and New Zealand "reviewed the toxicological database for ARA Single-cell Oil and determined that ARA Single-cell oil did

				not induce any histopathological, biochemical, or hematological changes that would be indicative of toxicity" at doses far higher than allowed for infant formula.) With regard to the safety of the consumption of the petitioned substance by infants (the extracted ARA) the *TR at lines 430-32,* stated: "Despite mixed results on many of the purported benefits of ARA supplementation in infant formula, adverse effects in infants fed formulas enriched with ARA/DHA have not been observed in randomized trials for up to one year." The TR noted that a now ten year old from 2001 study reported incidents of "flatulence, diarrhea, apnea, and jaundice in infants that were fed formulas with long-chain PUFA." *TR at lines 438-9* However, the TR did not did attribute these common infant ailments to any particular infant formula ingredient. To the extent these common infant ailments have been reported to FDA as "adverse events" arising from infant formula consumption, FDA's review has apparently concluded the events are *de minimis* in light of the nearly universal consumption of infant formula, and thus below the threshold of regulatory action. **Excessive Consumption** The TR cited one study that examined "the effect of increasing dietary ARA seven-fold" and concluded, "no effects on platelet aggregation, bleeding times, balance of vasoactive metabolites, serum lipid levels, or immune response were observed" *TR at lines 438-9* In addition, after review of a meta-analysis of 25 case-control studies evaluating a variety of effects, the TR concluded: "No effects in humans at high ARA doses were identified." *See TR at lines 438-9* **Absence of Contaminants** The TR accepted the data provided by Petitioner that was also provided to the FDA and concluded: "No residues of heavy metals or other contaminants have been reported in ARA Single-cell Oils at levels higher than FDA tolerances." *See TR at lines 378-9* The TR also accepted as unrebutted by other literature the finding that no solvent used in processing the ARA oil was detectable in the final product, and that the sole study in the scientific literature that tested more than 40 conventional (non-organic) vegetable oils for residues from processing solvents found no residue at an actionable level. *See TR at lines 386-90* **Global Regulatory Treatment on Safety** Because organic authorities do not assess food safety generally, the TR surveyed a few jurisdictions to assess the regulatory treatment by agencies charged with safety evaluations. Of course, the TR noted that the substance is recognized as GRAS in the U.S. *See e.g. TR at lines 90-92* (petitioned substance is GRAS); *TR, at lines 616-17* (noting one GRAS petition that cited 5 safety studies)

				The petitioned substance has been evaluated from a safety perspective by several countries and multi-lateral institutions. *See e.g. TR at lines, 459* (citing Australia and New Zealand). In particular, the TR noted that in Canada approved the petitioned substance "after assessing the toxicology, chemistry, microbiology, and nutrition of ARASCO® as a food ingredient." *See TR at lines 185-89* Other regulatory approvals for the petitioned substance for use in infant formula include, Australia, New Zealand, China, France, and the Netherlands—of note also, the European Union similarly allows "ARA Single-cell Oil from *M. alpina*" in infant formula. *See TR at lines* 190-93 Lastly, the TR noted that the petitioned substance would fall under Codex's general rule for food grade oils that allows their use provided they are free of prohibited additives like coloring agents etc. *See TR at lines* 197-98 In the United States, ARA Single-cell Oil is proposed for addition to infant formula and other organic food products. *See TR at lines 141-143* ARA has not currently been petitioned for GRAS designation as an addition to food items other than infant formula. *See TR at lines, 573-4*
11. Is there an adverse effect on human health as defined by applicable Federal regulations? [205.600 b.3]		x		The TR concluded that there is no adverse human health impact under federal regulations. "ARA Single-cell Oil is considered by FDA as GRAS in infant formula when used in combination with docosahexaenoic acid (DHA)." *See TR at lines 90-92* Also, "ARA Single-cell Oil is generally recognized as safe for human consumption, even in vulnerable infant populations." *See e.g. TR at lines, 496-97*ARA is presently allowed for use solely in infant formula and growing-up milks. *See TR at lines, 650-51.* The TR plainly stated that the state of the science is that, "adverse effects in infants fed formulas enriched with ARA/DHA have not been observed in randomized trials for up to one year." *See TR at lines,* 431-32
12. Is the substance GRAS when used according to FDA's good manufacturing practices? [§205.600 b.5]	x			The TR concluded: "ARA Single-cell Oil is characterized as GRAS under three different names submitted by four different applicants" *See TR at lines 332-36* (citing Martek Biosciences (GRN No. 41), Mead Johnson Nutritionals (GRN No. 80), Abbott Laboratories (GRN No. 94), and Cargill, Inc. (GRN No. 326)) when used in term and preterm infant formula along with GRAS concentrations of DHA. In addition to GRAS status, when ARA oil appears as an ingredient in infant formulas, the manufacturers submit premarket notification to FDA under section 412 of the Federal Food, Drug, and Cosmetic Act (FFDCA). Section 412 of FFDCA describes the more stringent statutory requirements that apply to infant formula as compared to the regulation of other foods (FDA, 2006)
13. Does the substance contain residues of heavy metals or other contaminants in excess of FDA tolerances? [§205.600 b.5]		x		The TR described the production, extraction and purification method of the natural oil. *See TR lines 212-256.* The TR noted that the post-extraction and purification processes "remove any extraction and purification solvents from the oil," *see TR at lines 270-73,* and concluded that the removed

				solvents are typically "recycled and reused." *See TR at 271-2* Any other impurities such as "trace metals, and oxidation products" are "removed physically through filtration or addition of adsorbents" *See TR at lines 249-50* Lastly, the *TR* cited Petitioner's evidence at *line 273*: "No residual hexane from the extraction process has been detected in samples of ARA Single-cell Oil using methods with detection limits of 0.3 ppm." The TR also cited a single Swiss study that tested more than 40 non-organic vegetable oils that used a similar extraction technology for hexane residues and concluded that less than 13% had any detectable residue and the level was "below acceptable tolerances." *See TR at line 237*

[1]If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

Category 2. Is the Substance Essential for Organic Production? Substance Arachidonic acid single-cell oil (ARA)

Question	Yes	No	N/A[1]	Documentation (TAP; petition; regulatory agency; other)
1. Is the substance formulated or manufactured by a chemical process? [6502 (21)]	x			The TR concluded the fungus from which the petitioned substance is isolated is "produced naturally via fermentation" *line 260-63*, but the extraction process typically involves a "nonpolar solvent." *See TR at 263 (*"ARA Single-cell Oil is produced naturally via fermentation of *M. alpina* and some other single-celled organisms. However, to extract the ARA Single-cell Oil from the fungus, a nonpolar solvent (usually hexane) is used.") *See TR at* 260-63
2. Is the substance formulated or manufactured by a process that chemically changes a substance extracted from naturally occurring plant, animal, or mineral, sources? [6502 (21)]		x		The TR concluded that the petitioned substance is a non-synthetic. *See TR at line 286* ("ARA Single-cell Oil does not appear to be a synthetic substance."); *see also TR at lines 274-78* (Applying National Organic Standards Board (NOSB) Joint Materials and Handling Committee draft policy: "extraction with a synthetic not on the National List would not result in a material being classified as synthetic unless either the extraction resulted in chemical change or the synthetic remained in the final material at a significant level"(NOSB, 2010).")
3. Is the substance created by naturally occurring biological processes? [6502 (21)]	x			The TR concluded that the petitioned substance is the product of a biological process. *See TR lines 260-63*
4. Is there a natural source of the substance? [§205.600 b.1]	x			ARA is present in foods, but for use in infant formula, or as a supplemental micronutrient in adult food products, the ARA must be extracted by a chemical process. *See TR lines* 221-240 (noting extraction methodologies). "Chicken and eggs are the primary sources of ARA in the U.S. diet." *TR at lines, 660-61.*
5. Is there an organic substitute? [§205.600 b.1]				There are no known certified organic sources of the extracted ARA oil. *See TR lines 466-80* (citing no certified source of ARA oil) The *TR* noted that fish oil is not an acceptable substitute because (a) "fish oil is not an organic agricultural product per se" and (b) "[f]ish oil does not contain high levels of pre-formed ARA" thus it must be "supplemented with another source of ARA (e.g., egg phospholipid or ARA Single-cell Oil) to achieve a fatty acid profile for optimal nutrition" and (c) "fish oil contains high levels of EPA, which can result in adverse effects on growth of pre-term infants even at low concentrations." *See TR at lines, 475-80* The TR noted that using organic eggs as an ARA source is generally not commercially feasible because achieving an egg with sufficient phospholipids requires "feeding chickens the biomass of ARA-producing fungus." *See TR at lines, 468-72* The TR also noted this approach is generally considered "wasteful of resources because ARA contents in egg phospholipids are relatively low and most of the egg is often discarded after phospholipid extraction." (internal citations omitted) *See TR at lines, 303-07.* Based on the TR, the necessary chicken feed would not be organic because ARA

				producing fungus would have to be added to complete its nutrient profile and it is not an organic material at this time.
6. Is the substance essential for handling of organically produced agricultural products? [§205.600 b.6]	x			The petitioned substance is unique because it is the only plant-based source of ARA currently available and is the most widely used ARA source in conventional and organic infant formulas. *See e.g. TR at lines, 468-69* ("There are three main sources of ARA …for supplementing infant formula: ARA Single-cell Oil, fish oil, and egg phospholipids.") Unlike animal sources, such as eggs or animal flesh, ARA from fungal oil is vegetarian, carries no risk of containing harmful environmental contaminants that an animal may ingest, *see TR at line 212* (noting fungus is grown in flasks) and there is no literature suggesting this production methodology adversely impacts biodiversity. *See TR at lines 394-95* ("No information was found on the effect of ARA Single-cell Oil on the environment or biodiversity")
7. Is there a wholly natural substitute product? [§6517 c (1)(A)(ii)]		x		The TR concluded that there are "Three main sources of ARA …for supplementing infant formula: ARA Single-cell Oil, fish oil, and egg phospholipids." *See TR at lines, 468-69* The petitioned substance is the only plant-based source of ARA. *Id.* non-synthetic, non-agricultural substance under 205.605(a). *See TR 286* ("ARA Single-cell Oil does not appear to be a synthetic substance.") There is no plant-based agricultural substitute for the petitioned substance. *TR at lines, 657-665* (discussing common sources)*; TR at lines, 666* (noting " eggs, poultry, beef, some fish" are principle ARA sources.)
8. Is the substance used in handling, not synthetic, but not organically produced? [§6517 c (1)(B)(iii)]	x			The TR concluded the substance is a non-synthetic, non-agricultural substance. *See TR 286* ("ARA Single-cell Oil does not appear to be a synthetic substance.")
9. Is there any alternative to using the petitioned substance in terms of practices or other available materials? [§6518(m)(6)]		x		According to the TR, there are no other plant-based sources of ARA, thus there is no vegetarian alternative to the petitioned substance. *TR at lines, 657-665* (discussing common sources)*; TR at lines, 666* (noting " eggs, poultry, beef, some fish" are principle ARA sources in adult diet.) For infants, the adult sources are not alternatives. *See also Question 7*
10. Is there an "alternative[s] to using the substance in terms of practices" that would make the substance unnecessary? [§6518 (m)(6)]		x		The petitioned substance is a food additive and there are no "practices" that substitute for its presence.

[1]If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

Category 3. Is the substance compatible with organic production practices? Substance Arachidonic acid single-cell oil (ARA)

Question	Yes	No	N/A[1]	Documentation (TAP; petition; regulatory agency; other)
1. Is the substance compatible with organic handling? [§205.600 b.2]	x			The petitioned substance is not the product of an excluded method and is a non-synthetic according to the TR.
2. Is the substance consistent with organic farming and handling? [§6517 c (1)(A)(iii); 6517 c (2)(A)(ii)]			x	
3. Is the substance compatible with a system of sustainable agriculture? [§6518 m.7]			x	
4. Is the nutritional quality of the food maintained with the substance? [§205.600 b.3]	x			The petitioned use of ARA Single-cell Oil is as a nutritional food ingredient added to infant formulas. ARA Single-cell Oil is added to infant formula to increase free ARA levels in formula to those comparable to ARA levels in human breast milk. *TR at lines, 37-40*
5. Is the primary use as a preservative? [§205.600 b.4]		x		*TR at lines, 37-40*
6. Is the primary use to recreate or improve flavors, colors, textures, or nutritive values lost in processing (except when required by law, e.g., vitamin D in milk)? [205.600 b.4]		x		*TR at lines, 37-40*
7. Is the substance used in production, and does it contain an active synthetic ingredient in the following categories: a. copper and sulfur compounds;			x	The petitioned substance is not used in production.
b. toxins derived from bacteria;			x	The petitioned substance is not used in production.
c. pheromones, soaps, horticultural oils, fish emulsions, treated seed, vitamins and minerals?			x	The petitioned substance is not used in production.
d. livestock parasiticides and medicines?			x	The petitioned substance is not used in production.
e. production aids including netting, tree wraps and seals, insect traps, sticky barriers, row covers, and equipment cleaners?			x	The petitioned substance is not used in production.

[1]If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

Category 4. Is the commercial supply of an agricultural substance as organic, fragile or potentially unavailable? [§6610, 6518, 6519, 205.2, 205.105 (d), 205.600 (c) 205.2, 205.105 (d), 205.600 (c)]

Substance Arachidonic acid single-cell oil (ARA)

Question	Yes	No	N/A	Comments on Information Provided (sufficient, plausible, reasonable, thorough, complete, unknown)
1. Is the comparative description provided as to why the non-organic form of the material /substance is necessary for use in organic handling?			x	The substance is not petitioned for inclusion on 7 CFR §205.606
2. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate **form** to fulfill an essential function in a system of organic handling?			x	
3. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate **quality** to fulfill an essential function in a system of organic handling?			x	
4. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate **quantity** to fulfill an essential function in a system of organic handling?			x	
5. Does the industry information provided on material / substance non-availability as organic, include (but not limited to) the following: a. Regions of production (including factors such as climate and number of regions);			x	
b. Number of suppliers and amount produced;			x	
c. Current and historical supplies related to weather events such as hurricanes, floods, and droughts that may temporarily halt production or destroy crops or supplies;			x	
d. Trade-related issues such as evidence of hoarding, war, trade barriers, or civil unrest that may temporarily restrict supplies; or			x	

e. Are there other issues which may present a challenge to a consistent supply?			x	