ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

DRAFT OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION FOR REFINED OIL FROM BUGLOSSOIDES ARVENSIS

Applicant:	**Technology Crops International.**
Responsible Person:	**Peter Lapinskas**
EC Classification:	**2.2**

Introduction

1. On 26 June 2013, the Food Standards Agency accepted an application from Technology Crops International for refined oil from *Buglossoides arvensis* as a novel ingredient. A copy of the application was placed on the Agency's website for public consultation.

2. The applicant states that refined oil from the seeds of *Buglossoides arvensis* (RBO) is a rich source of omega-3 and omega-6 fatty acids, including the omega-3 fatty acid stearidonic acid (SDA), which is an intermediate in the synthesis of eicosapentaenoic acid (EPA) in the body from dietary alpha-linolenic acid (ALA). SDA is more efficiently converted to EPA than ALA and so dietary sources of SDA are important for individuals who are unwilling or unable to consume EPA directly (for instance from oily fish or fish oil supplements). There are other possible significant sources of SDA, but these are either more expensive and less concentrated (e.g. Echium oil) or not yet commercially available (e.g. SDA-rich oil from genetically modified soya beans). The applicant therefore considers that RBO has the potential to improve the nutritional status of a significant subsection of the population at a lower cost than currently available products.

3. RBO is closely taxonomically related, and is similar in composition, to Echium oil, which was approved as a novel food ingredient in the EU in 2008[1]. The applicant highlights that the fatty acid profiles of the two oils are similar, but with RBO having a higher concentration of SDA and ALA and a lower concentration of gamma linoleic acid (GLA).

4. The applicant intends that RBO will be incorporated into a range of foods and also in food supplements.

[1] Commission Decision 2008/558/EC of 27 June 2008,authorising the placing on the market of refined echium oil as novel food ingredient

5. RBO has been classified as a complex novel food from non-GM source, the source of the novel food has no history of food use in the EU (class 2.2) according to the scheme in Commission Recommendation 97/618/EC.

I. Specification of the novel food

6. The applicant has provided detailed specifications for its RBO as below. Analytical data show that three separate batches of RBO comply with their proposed specifications:

Parameter	**Proposed specification**	**Buglossoides oil batches**		
		NZ00053 Batch 4	NZ00056 Batch 5	NZ00058 Batch 6
Description	Buglossoides oil is the pale yellow product obtained by refining oil extracted from the seeds of *Buglossoides arvensis* (L.) I.M.Johnst.	Confirmed	Confirmed	Confirmed
Stearidonic acid content	Not less than 15% w/w of total fatty acids	20.5	19.7	20.8
Trans fatty acids	Not more than 2% w/w of total fatty acids	<1.0	<1.0	<1.0
Acid value	Not more than 0.6 mg KOH/g	0.22	0.12	0.34
Peroxide value	Not more than 5 meq O_2/kg	2.03	1.55	1.22
Unsaponifiable content	Not more than 2%	0.28	0.43	0.73
Protein content (total nitrogen)	Not more than 20 µg/mL	1.3	1.0	1.3
Pyrrolizidine alkaloids	Not detectable with a detection limit of 4 µg/kg	<1	<1	<1

7. RBO consists primarily of triglycerides (about 90%) with smaller proportions of diglycerides, monoglycerides and free fatty acids (2 – 6%, 2 – 4% and <0.3% respectively). The remaining part of the oil consists of the non-saponifiable fraction (<2%) which contains a range of sterols and tocopherols.

8. The applicant states that pyrrolizidine alkaloids (PAs) have been found to occur in a number of species in the Boraginaceae family, including *Buglossoides arvensis*. The applicant highlights that PAs are water-soluble

and therefore the majority of any PAs present in *Buglossoides arvensis* seed would be expected to remain in the seed meal on extraction, and the level in the oil will be further reduced during refining. The applicant reports that a sample of unrefined Buglossoides oil was analysed and found to contain 44 µg/kg of PAs, but refining reduced this level to below 1 µg/kg.

9. The applicant has also considered other inherent constituents which might potentially give rise to toxicity (oxidation products, hydrolysis products, trans fatty acids and erucic acid). Based on analyses data, the applicant concludes that all were found to be present at well below regulatory limits. Additionally, no significant external contaminants were detected in RBO from analyses for pesticides, elemental contaminants, dioxin and dioxin-like polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), melamine and cyanuric acid.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

II. Effect of the production process applied to the novel food

10. The applicant has provided details of the production process. RBO is extracted from the seeds of *Buglossoides arvensis* by mechanical pressing and solvent extraction or solvent extraction alone with hexane or isohexane. Extraction is followed by a series of refining steps such as degumming, addition of sodium hydroxide to neutralise free fatty acids, bleaching and filtration. Some refining steps such as deodorisation after bleaching are optional and are carried out to ensure that RBO batches meet the required specifications.

11. The applicant has acknowledged the issue of stability of RBO, particularly focusing on oxidative stability. A study was conducted to assess the stability of RBO at different temperatures (4, 22 and 60°C) for twelve weeks, using peroxide value as a measure of stability. Results show that the oil remains within specification for peroxide value over the twelve weeks at all temperatures. The applicant concludes that RBO is stable, even when stored under extreme conditions and that the oil is sufficiently stable to be used in consumer products with appropriately calculated shelf lives.

***Discussion**: The Committee requested further details on the seed harvesting procedure that is used and the steps that are taken to ensure the absence of other plant material. The applicant reported that stringent procedures are in place to ensure the purity of planted seed (the total amount of impurities is limited to 2%, the same level that has been widely adopted for other crops in the UK such as rapeseed). Harvesting is carried out in a similar manner to*

other oilseed crops and using the same equipment. The harvested seed is cleaned to remove other plant fragments prior to oil production.

The Committee additionally requested reassurance about the homogeneity of the seeds used as the source material for the refined oil. The applicant noted that inhomogeneity of seeds could arise from genetic variability or environmental factors. The first of these is minimised by sowing a uniform genetic strain. The latter is normal for all crops and can result in differences between batches of the oil that require further processing, for example to adjust colour or acid value.

The Committee also queried the concept of employing additional optional steps in processing RBO until it meets the required specifications, the main concern being whether this allows a potentially unsafe product to be re-processed to make it fit for consumption. The applicant pointed out that the manufacturing and refining process for RBO is equivalent to the processes that are used for all major food oils and is designed to use the minimum number of steps which will provide a product that meets the required specifications. Additional processing can be used to standardise colour and acid value, or to reduce levels of waxes or minerals. The applicant clarified that any batches that cannot be brought up to the specification standards are rejected and destroyed.

The Committee was satisfied that all its questions had been addressed and no further information was requested.

III. History of the organism used as a source of the novel food

12. The applicant states that *Buglossoides arvensis* was first described and classified as *Lithospermum arvense* by Linnaeus (1753). It has been described more recently by Clapham et al. (1961). The plant is native to the UK and is found in many parts of Europe and North America.

13. The applicant states that the safety of RBO is supported by consideration of the safety of its constituents, which are found in a wide range of other food products and which have been tested in both animals and humans, as well as by studies on the whole oil in animals.

14. The applicant also highlights that refined Echium oil, which is also a triglyceride vegetable oil and which contains all the fatty acids present in RBO, in similar proportions, has been approved as a novel food ingredient in the EU since 2008.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

IX. Anticipated intake/extent of use of the novel food

15. RBO is similar in composition to Echium oil with the exception that the proportions of SDA and ALA are higher in RBO. Echium oil has been approved as a novel food in the EU and estimates of the anticipated intake were provided in the dossier which accompanied the application made by Croda Chemicals Ltd.

16. The applicant proposes that RBO should be used in exactly the same foods and in such proportions as to give the same maximum quantities of SDA as are already approved for Echium oil. As such, the applicant has used the intake estimates provided for refined Echium oil as a basis to estimating RBO intake. The applicant's aim is to provide approx. 200mg of SDA per daily serving.

17. Male adults were calculated to have the greatest mean and 97.5th percentile intakes of SDA at 1128 and 2175 mg/day, while children had the lowest at 719 and 1351 mg/day. On a body weight basis, children were calculated to have the highest intakes, with daily SDA intakes of 51 mg/kg body weight (mean) and 103 mg/kg body weight (97.5th percentile). Female adults had the lowest intakes at 13 and 26 mg/kg body weight/day. These figures represent an overestimate of the likely consumption of SDA, because not all of the food groups used in compiling the original estimates were included in the final approval for Echium oil.

18. In the group with the highest intake (male adults), estimated consumption of SDA did not exceed 2200 mg SDA/person/day, equivalent to 11 servings of food at the maximum level of incorporation of the oil. Mean consumption was estimated at 1128 mg SDA/person/day, equivalent to 5-6 daily servings. This is likely to be a significant overestimate of actual intakes as it would be extremely unlikely for a person to choose so many products, all with the maximum levels of incorporation of the oil.

19. The applicant states that the safety studies discussed in the dossier (where intakes of up to 4200 mg SDA/person/day were tested) indicate that it is safe to consume SDA at the highest estimated consumption level of 2200 mg/person/day.

20. The applicant has explained that both SDA and ALA levels will be comparable in RBO-containing foods and in foods containing Echium oil, but the added quantity of RBO will be lower as it contains higher concentrations of both fatty acids.

21. RBO is intended to be added to the following foods at levels of incorporation up to the specified maxima.

Table: Intended uses and incorporation levels of refined Buglossoides oil (Food categories are consistent with Part E of Annex II to Regulation 1333/2008 on Food Additives)

Use group	Maximum level of stearidonic acid
Dairy products and analogues (Category 1)	250 mg/100 g; 75 mg/100 g for drinks
Cheese and cheese products (Category 1.7)	750 mg/100 g
Butter (Category 2.2.1) and other fat and oil emulsions including spreads (Category 2.2.2)	750 mg/100 g
Breakfast cereals (Category 6.3)	625 mg/100 g
Food supplements as defined in Directive 2002/46/EC of the European Parliament and of the Council excluding food supplements for young children (Category 17).	500 mg/daily dose as recommended by the manufacturer
Dietary foods for special medical purposes as defined in Directive 1999/21/EC excluding dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC (Category 13.2)	In accordance with the particular nutritional requirements of the persons for whom the products are intended
Dietary foods for weight-control diets intended to replace total food daily intake or an individual meal (Category 13.3).	250 mg/meal replacement

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

XI. Nutritional information on the novel food

22. The applicant intends that RBO will primarily be a replacement for Echium oil as it will be cheaper (due to the higher yielding nature of the crop). RBO also has a higher proportion of SDA, so that less oil is required to provide the same intake of SDA.

23. The applicant states that both RBO and Echium oils are more expensive than fish oils, so it is unlikely that consumption of fish oils as a source of omega-3 fatty acids will be significantly reduced by introduction of RBO onto the EU market. The applicant points out that RBO is most likely to be consumed by those looking to increase their intake of long-chain omega-3 fatty acids but who

are unwilling or unable to consume fish oils either for dietary reasons (e.g. vegetarians) or because they do not like the taste of fish or are concerned about the possible presence of marine pollutants.

24. The applicant suggests that both Echium oil and RBO may be preferable to other current plant-based sources of omega-3 fatty acids such as linseed and hempseed, as they contain significant levels of SDA in addition to ALA. The conversion of ALA to EPA is much less efficient than the conversion of SDA, requiring greater quantities of these other oils to be consumed to achieve equivalent EPA production in the body.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

XII. Microbiological information on the novel food

25. The applicant states that microbiological contamination of RBO is unlikely to be of concern. The processes used to extract and refine RBO include temperatures in excess of 90°C under vacuum for tens of minutes, and filtration at the micron level. The oil itself has a very low water content and activity and so does not support subsequent microbial growth. The applicant has presented microbiological analyses confirming the absence of microbial contamination (yeasts, moulds, Enterobacteria, *S.aureus*) in three separate batches of RBO.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

XIII. Toxicological information on the novel food

26. The applicant has summarised a number of toxicological studies on a range of different oils. The three most relevant studies relate to the applicant's own RBO.

27. Two sub-chronic mouse feeding studies (28 days and up to 56 days) are described, where the applicant's RBO (3.9 mg/kg body weight per day) was incorporated into the diet of mice. The applicant states that there were no treatment related adverse effects.

28. A sub-chronic (56 day) toxicity study conducted with salmon fry where the applicant's RBO was incorporated into the diet at 11.5%. No adverse effects were reported.

29. The applicant states that the metabolic fate of RBO is well understood and does not give any cause for concern. The component fatty acids are released

from the glycerides upon digestion and are used primarily as an energy source. The essential fatty acids can also be metabolised to longer chain or more unsaturated fatty acids. ALA and SDA can be elongated and desaturated to EPA, the omega-3 fatty acid typically found in fish oils. SDA has not been found to accumulate in human or animal tissues.

Discussion: The Committee requested full study reports for certain studies summarised in the dossier that highlight "no compound related adverse effects", in order to evaluate these data independently: Surette & Matar, 2012 (using the applicant's RBO); Engler, 1993 and Harris et al., 2007 (using other SDA-containing oils). The applicant has clarified that it does not have access to the original data or unpublished material from these studies so only the published papers were evaluated.

Similarly, full study reports were requested for two rodent feeding studies with substances other than RBO, to evaluate some of the reported findings and their implications for humans (Engler, 1993 and Wainwright et al., 2003). Additionally, the applicant has provided further reassurance in its response as to why reported findings from the study by Wainwright et al., 2003 are not a cause for concern with respect to the gamma-linoleic acid (GLA) component of RBO.

Given that neither RBO nor its source material has any history of consumption, the Committee enquired whether any human study data are available or whether any clinical studies are underway. The applicant confirmed that no human study data are available and no clinical studies are underway and provided the following reasoning as to why such data are not necessary.

- *RBO is a highly purified vegetable oil with a restricted number of components, which have been well characterised and all appear in common foods that are widely consumed in the EU.*
- *RBO is extremely similar in composition to refined Echium oil (which is approved in the EU as a novel ingredient).*
- *The applicant has obtained GRAS (Generally Regarded As Safe) status for its RBO in the USA and the Expert Panel involved in this assessment concluded unanimously on the safety of this novel ingredient for the same intended uses described in this application.*
- *The applicant proposes to launch RBO-containing foods onto the US market in the first instance, with a view to expanding to the EU market at a later stage. The applicant mentions that it is likely there will be a significant level of experience with human intake of RBO before it is introduced onto the EU market.*

The Committee was satisfied that there are no apparent safety concerns relating to this novel ingredient or its known constituents and was content that it is not necessary to conduct a human study to obtain further data.

The Committee noted that neither the novel ingredient nor its source has a history of consumption anywhere in the world. The Committee therefore recommends that the applicant should ensure that reports of adverse reactions are closely monitored after the product is introduced to the market, in order to identify any unexpected effects [Note: the Committee is currently discussing with the applicant how this might done].

Allergenicity and labelling

30. Pollen from *Echium vulgare* has been reported to contain cytochrome C allergenic proteins. In order to ensure that Echium oil would not provoke an allergic reaction in sensitive individuals, a limit on the total protein content of 20 µg/ml was included in the 2008 authorisation decision. The applicant states that no allergens have been reported in *Buglossoides arvensis*, which suggests that it may not have the same allergenic potential. However, the applicant proposes that the protein content of RBO should also be limited to 20 µg/ml, in order to avoid possible unexpected allergic reactions.

31. The applicant assessed protein levels in RBO using a combustion / chemiluminescence method, which failed to find any protein at the level of detection (<10 µg/ml total N).

32. The applicant also conducted further analyses using the borate extraction method and the CBQCA analytical procedure using a commercial analytical kit as described by Rigby et al. 2011. The results from the analyses of three separate batches show that the protein content of RBO is 1-1.3 µg/ml, substantially below the proposed limit of 20 µg/ml.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

CONCLUSION

The ACNFP has completed its assessment of RBO as a novel ingredient to be added to a range of foods and did not identify any significant safety concerns relating to this ingredient. On request, the Committee received further information from the applicant on the following:

- The production process
- The potential implications of optional processing steps
- Further details on certain toxicology studies
- Whether human study data are available

After reviewing the applicant's response to these issues, the Committee did not have any outstanding safety concerns.

The Committee noted that neither the novel ingredient nor its source has a history of consumption anywhere in the world and as a result recommended that the applicant should ensure that reports of adverse reactions are closely monitored after RBO-containing products are introduced onto the market.

The ACNFP therefore concluded that RBO meets the criteria set out in Article 3(1) of Regulation (EC) No 258/97, namely it does not:

- present a risk to the consumer
- mislead the consumer
- differ from foods or food ingredients which it is intended to replace to such an extent that its normal consumption would be nutritionally disadvantageous for the consumer.

DRAFT December 2013