GENERALLY RECOGNIZED AS SAFE (GRAS) NOTICE FOR MYCOPROTEIN AS A FOOD INGREDIENT

3F BIO Limited

June 02, 2020

GENERALLY RECOGNISED AS SAFE (GRAS) STATUS FOR ABUNDA® MYCOPROTEIN AS A FOOD INGREDIENT

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Part 1. SIGNED STATEMENTS AND CERTIFICATION

Pursuant to 21 C.F.R. Part 170, subpart E, 3F BIO Ltd submits a Generally Recognized as Safe (GRAS) notice and claims that the use of ABUNDA® mycoprotein in foods, as described in Parts 2 through 7 of this GRAS notice, is not subject to the premarket approval requirements of the FD&C Act based on its conclusion that the substance is GRAS under the conditions of its intended use.

The objective of this notification is to show that ABUNDA® mycoprotein is generally recognised as safe (GRAS) for its intended use. This conclusion is largely based on the fact that this product as produced by the notifier is substantially the same in composition to mycoprotein that is currently on the market, which is manufactured by the previous notifier (GRAS No. 91), under identical conditions of intended use, using the same strain and through an equivalent manufacturing process.

1.A Name and address of the notifier

Contact person: Sofia Mavromati

Company name: 3F BIO Limited

Address: Registered office: 163 Bath Street, Glasgow, G2 4SQ, United Kingdom,
Trading Address: 135 Buchanan Street, 4.1, Glasgow, G1 2JA, United Kingdom

1.B Common or Trade Name

The common name is mycoprotein. The trade name is ABUNDA mycoprotein. Details about the identity of the notified substance appears in the document following.

1.C Applicable Conditions of Use of the Notified Substance

1.C.1 Foods in Which the Substance is to be used

The intended use and use levels of ABUNDA mycoprotein are the same as GRN No. 91, which has been filed in the GRAS inventory with a “no questions” FDA letter. The existing GRAS substance is already in commercial use in the United States.

3F BIO is intending to supply the notified substance for use in a variety of products as an alternative to meat. For example, ABUNDA mycoprotein may be used in vegetarian and vegan Burgers and vegetarian and vegan sausages. Exclusions from its intended use are meat products, poultry products, and infant formula.

1.C.2 Levels of Use in Such Foods

3F BIO is intending to supply ABUNDA mycoprotein to the market on a Business to Business (“B2B”) basis.

Product concept development activities suggest that the substance will be present in final products in varying amounts, up to 90% in the final product.

1.C.3 Purpose for Which the Substance is Used

The notified substance is intended to be used as a meat substitute.

1.C.4 Description of the Population Expected to Consume the Substance

The population expected to consume the substance consists of members of the general population who consume at least one of the products described above.

1.D Basis for the GRAS Determination

This GRAS determination is based on the data generally available in the public domain and scientific procedures pertaining to the safety of the following:

- Existing mycoprotein products.
- Establishing equivalence of ABUNDA mycoprotein to the existing mycoprotein.
- Specification of raw materials to manufacture ABUNDA mycoprotein.
- Standardised processing conditions applied to produce ABUNDA mycoprotein.
- Contaminants analysis of ABUNDA mycoprotein.

1.E Availability of Information

The data and information that forms the basis of this ABUNDA mycoprotein GRAS determination is available for the Food and Drug Administration's review. If additional information is required, it can be provided based on a request by the FDA to 3F BIO's registered address:

3F BIO Ltd, 163 Bath Street, Glasgow, G2 4SQ, United Kingdom

1.F Availability of FOIA Exemption

None of the data and information in Parts 2 through 7 of this GRAS notice are considered exempt from disclosure under the Freedom of Information Act (FOIA) as trade secret or commercial or financial information that is privileged or confidential.

1.G Certification

We certify that, to the best of our knowledge our GRAS notice is a complete, representative, and balanced submission that includes unfavourable information, as well as favourable information, available and appropriate to the evaluation of the safety and GRAS status of the use of the notified substance, i.e. ABUNDA mycoprotein.

Signature 

_____ **June 02, 2020**

Name: Jim Laird; Date

Title: CEO, Director, 3F BIO Ltd

Please address correspondence to:

Sofia Mavromati, Food Safety and Quality Manager, 3F BIO Ltd
Email: sofia.mavromati@3fbio.com; mobile: +44 (0) 776 7412 809 (M)

Signature

Sofia Mavromati

June 02, 2020
Date

1.H FSIS/USDA Statement

3F BIO Ltd does not intend to add mycoprotein to any meat and/or poultry products that come under USDA jurisdiction. Therefore, 21 CFR 170.270 does not apply.

Part 2. IDENTITY, METHOD OF MANUFACTURE, SPECIFICATIONS, AND PHYSICAL OR TECHNICAL EFFECTS OF THE NOTIFIED SUBSTANCE

2.A Scientific Information About the Identity of the Notified Substance

2.A.1 Scientific Information Sufficient to Identify the Biological Source

Mycoprotein is derived from the cultivation of a strain of fungi, *Fusarium venenatum.* The strain of *F. venenatum* relating to GRAS No. 91 was deposited (originally as *Fusarium graminearum* A 3/5) [1,2] in a national culture collection by RHM Research, Ltd. It has strain designation IMI145425.

The same micro-organism is used for ABUNDA mycoprotein, and the source of the master culture used by 3F BIO is from ARS Culture Collection. ARS Culture is one of the largest public collections of microorganisms in the world, containing approximately 98,000 isolates of bacteria and fungi[3].

3F BIO has followed standard industrial best practices[4] to maintain the purity and integrity of the starter cultures derived from the original culture collection material. In particular:

- Seed cultures are prepared from vials of *F. venenatum* generated from the original culture supplied by ARS Culture Collection.
- These are prepared as glycerol suspensions or spore stocks which are stored at -80°C until required to prepare the actual inoculum for the start of fermentation.
- Traceability to the original reference material can be demonstrated.

[1] Yoder W.T. and Christianson L.M. 1998. Species-Specific Primers Resolve Members of Fusarium Section Fusarium. Taxonomic Status of the Edible ‘‘Quorn’’ Fungus Re-evaluated. Fungal Genetics and Biology, 23, 68-80.
[2] O’Donnell K, Cigelnik E., and Casper H. H. Molecular Phylogenetic, Morphological, and Mycotoxin Data Support Reidentification of the Quorn Mycoprotein Fungus as Fusarium venenatum. Fungal Genetics and Biology 23, 57–67
[3] https://nrrl.ncaur.usda.gov/
[4] 3FBIO internal document – 3F Bio BBEPP Technology Transfer Doc.

2.A.1.1 Common Name

Mycoprotein, or mycoprotein derived from *Fusarium venenatum*.

2.A.1.2 Chemical Name

Not applicable.

2.A.1.3 Chemical Abstract Service (CAS) Registry Number

Not applicable.

2.A.1.4 Empirical Formula

Not applicable.

2.A.1.5 Molecular Weight

Not applicable.

2.A.1.6 Structural Formula

Not applicable.

2.A.1.7 Background

3F BIO™ intends to manufacture and sell ABUNDA® mycoprotein as a food ingredient, derived from the aerobic fermentation of *Fusarium venenatum*.

Mycoprotein derived from this micro-organism was originally placed on sale in the United Kingdom in 1985 and since then it has been sold in a number of countries in the EU and worldwide including the US.

2.A.2 Potential Toxicants in the Source of the Notified Substance

Under this heading the following were considered:

- Ribonucleic acid (RNA);
- Heavy metals;
- Mycotoxins;
- Pesticides;
- Allergens.

3FBIO has risk assessed[5] the potential for these groups of compounds and has established appropriate specifications to ensure that any contribution to risk for potential toxicants by raw materials is minimised. The remainder of the section discusses available evidence to demonstrate that, if present, any undesirable substances associated with the production process are so low as to be unlikely to present a risk to the consumer.

RNA: Growth of *F. venenatum* naturally results in a product with a high purine content, much of it in the form of ribonucleic acid (RNA). The RNA (and hence purine) content of both mycoprotein originally on the market and ABUNDA is substantially reduced to < 2% dry matter weight by post fermentation heat treatment steps. Increasing the temperature induces the fungus to produce RNA hydrolysing enzymes (RNase) which break down the RNA into its component nucleotides. These diffuse out of the mycelial mass, enter into solution and are removed during the centrifugation process.

Most foods in the diet contain purines to one degree or another since they are synthesised by all organisms. In humans the end-product of their catabolism is uric acid which is generally excreted in the urine. In some individuals the uric acid load is so great that the compound cannot be excreted effectively and as a result comes out of solution and crystallises in different parts of the body. Uric acid accumulation in the joints leads to the clinical condition of gout[6]. Long term treatment of gout and other uric acid related diseases involves consuming an appropriate diet[7]. As a result of the processes used, the UK Gout Society has identified both mushrooms and mycoprotein as, 'moderate purine foods' that can be eaten, 'in moderation'[8].

Heavy metals: A comparison of typical heavy metal values for mycoprotein originally on the market in the original GRN No. 91and the notified substance is presented in Table 1. Consideration of these data demonstrate that levels of heavy metals are equivalent or lower than those previously reported and below the relevant MRL's (maximum residue limits) established in European Union chemical contaminants legislation (Commission Regulation (EC) No 1881/2006).

Table 1. Comparison of typical heavy metal levels reported in GRAS No. 91 with those obtained for ABUNDA® mycoprotein

Heavy metal ***(mg/kg dry weight)***	**Existing Mycoprotein** [(1)]	**ABUNDA® Mycoprotein** [(2)]
Arsenic	< 0.1	0.03
Cadmium	< 0.1	0.01
Lead	< 0.1	0.04
Mercury	< 0.1	0.01

[(1)] Sourced from GRAS No. 91
[(2)] 3FBIO internal data

[5] Discussed in 3FBIO internal document Ref. FS02-D-002
[6] Seegmiller, J.E., Grayzel, A.I., Laster, L. and Liddle, L., 1961. Uric acid production in gout. The Journal of clinical investigation, 40(7), 1304-1314.
[7] https://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/gout-diet/art-20048524
[8] http://www.ukgoutsociety.org/docs/goutsociety-allaboutgoutanddiet-0113.pdf

Mycotoxins: Mycotoxins are the toxic metabolites of certain fungi; some *Fusarium* spp. are known to produce these compounds under particular growth conditions. The strain of *F. venenatum* used was selected in part due to its inability to produce mycotoxins of concern.

3F BIO has submitted 7 non-consecutive campaigns of mycoprotein for testing, not only for the presence of known *Fusarium* spp. mycotoxins but also for other mycotoxins of regulatory significance produced by other fungal genera (Aflatoxin B_1, total aflatoxins and ochratoxin A).

As shown in Table 2, levels of mycotoxin were lower than the limit of detection for each of the mycotoxins considered.

Table 2. Comparison of typical mycotoxin levels reported in GRAS No. 91 with those obtained for ABUNDA® mycoprotein

Mycotoxins ***(µg/kg wet weight)***	**Existing Mycoprotein [(1)]**	**ABUNDA® Mycoprotein [(2)]**
Aflatoxin B_1	Not reported	Not detectable
Total aflatoxins (Sum B1, B2, G1, G2)	Not reported	Not detectable
Ochratoxin A	Not reported	Not detectable
HT2 & T2	Not reported	Not detectable
Deoxynivalenol (DON)	Not detectable	Not detectable
3-acetyl-DON	Not detectable	Not detectable
Nivalenol	Not detectable	Not detectable
Diacetoxyscirpenol	Not detectable	Not detectable
Fusarenon	Not detectable	Not detectable
Neosolaniol	Not detectable	Not detectable
15-acetyl-DON	Not reported	Not detectable
Fumonisin B1	Not reported	Not detectable
Fumonisin B2	Not reported	Not detectable
Zearalenone	Not reported	Not detectable

[(1)] Sourced from GRAS No. 91
[(2)] 3FBIO internal data

2.B Method of Manufacture

3F BIO manufactures an ingredient (trade name ABUNDA®) which is a protein-rich preparation (mycoprotein) derived from the micro-organism *Fusarium venenatum*. It is produced using an

aerobic fermentation process, from a food grade carbohydrate substrate. The organism is unchanged from its natural state and has not been subject to any form of genetic manipulation[9].

3F BIO's technology integrates with a 1st generation ethanol biorefinery to create an efficient zero waste process but where this integration does not alter the core process of producing mycoprotein. Once separated from the fungal biomass, which constitutes the product, the partially spent media stream from the fermentation process producing mycoprotein contains non fermented sugars and proteins, and by integrating these into the ethanol production process this creates a zero-waste process for manufacturing mycoprotein and an overall more efficient and environmentally sustainable process.

The process maintains the core aspects of the legacy fermentation process using the same strain and feedstock as those detailed in the GRAS notice submitted to the FDA in 2001.

The figure below outlines the main steps of the manufacturing process for ABUNDA mycoprotein:

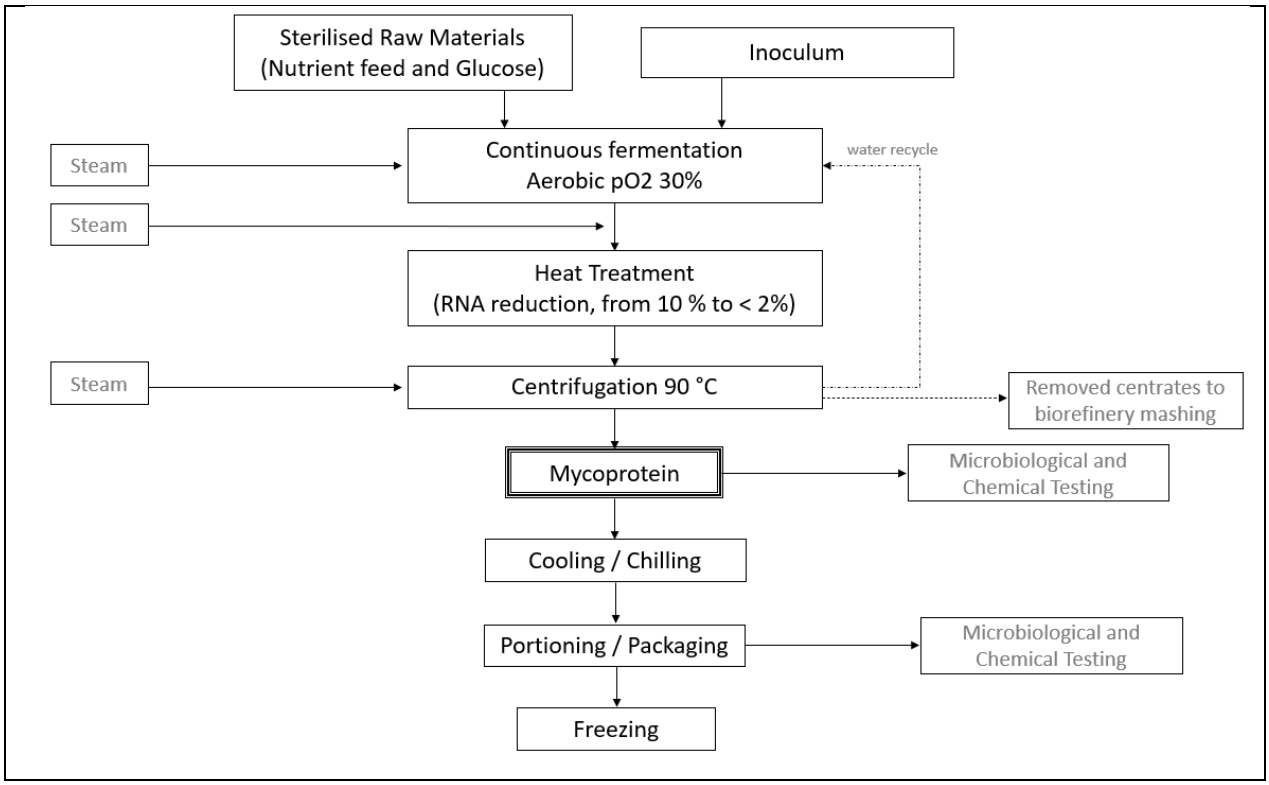

Figure 1. Flow chart of Manufacturing Process

List of raw materials:

- *Fusarium venenatum*
- Refined glucose or glucose syrups
- Deionised water

AND:

[9] 3FBIO internal document FS02-D-001.

Table 3. List of nutrients used in the manufacturing process of ABUNDA mycoprotein

Chemical Formula	Substance Name	Legislation	Approved Food Additive (Y/N)
H_3PO_3	Phosphoric Acid	FDA Substances Added to Food	Y
$Ca(C_2H_3O2)_2$	Calcium Acetate	FDA Substances Added to Food	Y
$MgSO_4$ 7 H_2O	Magnesium sulfate heptahydrate	EC 1925/2006	Y
$CaCl_2$ 2 H_2O	Calcium Chloride dihydrate	EC 1129/2011	Y
K_2SO_4	Potassium sulfate	EC 1129/2011	Y
$ZnSO_4$ 7 H_2O	Zinc (II) sulfate heptahydrate	EC 1925/2006	Y
$MnSO_4$ H_2O	Manganese (II) sulfate monohydrate	EC 1925/2006	Y
$CuSO_4$ 5 H_2O	Copper (II) sulfate pentahydrate	EC 1925/2006	Y
$FeSO_4$ 7 H_2O	Iron (II) sulfate heptahydrate	EC 1925/2006	Y
$C_{10}H_{16}N_2O_3S$	Biotin	FDA Substances Added to Food	Y
$C_5H_{14}ClNO$	Choline Chloride	JECFA Approved	Y
NH_4OH	Ammonium hydroxide (25%)	FDA Substances Added to Food	Y
$FeCl_3$ 6 H_2O	Iron (III) chloride hexahydrate	EU 2015/1739 [(a)]	Y
Citric acid H2	Citric acid monohydrate	EC 1129/2011	Y
ZnCl2	Zinc chloride	EC 1925/2006	Y
MnCl2 4 H2O	Manganese (II) chloride tetrahydrate	EC 1925/2006	Y
CuCl2 2 H2O	Copper (II) chloride dihydrate	EC 1925/2006	Y
CoCl2 6 H2O	Cobalt (II) chloride hexahydrate	EFSA Opinion 2009 [(b)]	Y
Na2MoO4 2 H2O	Disodium molybdate dihydrate	EC 1925/2006	Y
KH2PO4	Potassium dihydrogen phosphate	FAO/WHO Food Additive Evaluations (JECFA)	Y
NH4Cl	Ammonium chloride	41st CAC 2018	Y

Notes:

[(a)] EFSA assessment of the safety of cobalt (II) chloride hexahydrate added for nutritional purposes as a source of cobalt in food supplements and the bioavailability of cobalt from this source.

[(b)] EFSA Scientific Opinion on the safety of the complexation product of sodium tartrate and iron (III) chloride as a food additive

2.B.1 Nutrient solution preparation

- Nutrient salts will be added to agitated vessels.
- The stock solution would either be prepared with fresh or recycled water or combinations thereof.
- The use of water recycle within the mycoprotein fermenter feed preparation reduces the amount of fresh dilution water required.
- Nutrient salts/trace metals require continuous sterilisation (excluding ammonia solution)
- The total weight of Potassium Sulphate; Magnesium Sulphate, Calcium Acetate, and Iron Sulphate will be at an appropriate strength solution made up with glucose feedstock, and trace elements.

Potable water will be used for process make up.

2.B.2 Heat sterilisation of Feedstock

- Mycoprotein fermentation is operated under monoseptic conditions.
- Continuous thermal sterilisation - sterilises combined streams of glucose, inorganic nutrients and water through heat exchangers.
- A standard design of sterilisation unit with a typical serpentine holding section would be anticipated
- Unit inlet temperature would be determined by the resultant mix of glucose solution feedstock (60°C); water, and centrates recycle (up to 90°C).
- The sterilised feed would be cooled to feed to the fermenter and/or storage vessel.

2.B.3 Aerobic Fermentation

- Fermenter design – stainless steel, stirred tank reactors will form both the seed and production fermenters. This is standard fermentation technology and is well documented in literature.
- The fermenter operates with temperature control to maintain 30°C, pH control to pH 6 using ammonium hydroxide and dO_2 > 0% via cascade control of impeller rpm and airflow to the sparger (in vvm).
- The continuous culture is maintained for up to c.30 days at which point the batch is terminated.
- Fermenters (and ancillaries) will be of good hygienic design using best practice.
- Sterilisation will be achieved between continuous culture batches by steam sterilisation (SIP) to approximately 125°C.
- Cleaning in place ("CIP") will be achieved by typical cleaning solutions at 70°C i.e. 2-3% NaOH.
- The fermenter off-gas will go through odour abatement if required.
- Compressed air quality that comes into direct contact with the product is in accorance ISO 8573-1:2010.

2.B.4 RNA Heat Treatment

- Carried out to reduce the RNA content of biomass from approx 10% to < 2% (w/w) on dry basis.
- Rapid heating of the fermentation broth in a continuous manner from 30°C to 68-73°C, followed by a hold time of minimum 15 minutes.
- The heat treatement has been shown to deactivate the organism therefore redendering it as *"non-viable"*.

2.B.5 Mycoprotein separation

- Biomass slurry is heated further to approximately 85-95°C then centrifuged.
- The paste is isolated with an approximate composition of 25% dry biomass and 75% water.

2.B.6 Quality Assurance

ABUNDA mycoprotein is manufactured under Good Manufacturing Practices ("GMP") using common food industry materials and processes in accordance with the applicable parts of 21 CFR, part 110 of the Code of Federal Regulations. 3F BIO utilises the principles of Hazard Analysis and Critical Control

Point ("HACCP") in the manufacturing process and rigorously tests its final production batches to verify adherence to quality control specifications.

3F BIO has established raw material specification as part of its supplier assurance programme to ensure final product quality. Standard operating procedures are followed to ensure integrity. Several samples are kept for analysis should process deviations be observed. The temperature of heat sterilization is continuously monitored and controlled.

The control of an axenic, well aerated, nutrient rich fermentation broth is important to ensure pathways for secondary metabolite production are not activated and mycotoxins are not produced. Tight control over nutrient and oxygen levels in the fermenter ensure no mycotoxins are produced, and regular testing of final product allows for safe release.

A quality system has been developed which incorporates interdependent elements of quality control and quality assurance and any changes are controlled within this quality system.

3F BIO has generated data from a minimum of 7 pilot production campaigns and analysis of multiple samples demonstrated there are no significant changes in protein quality from the exiting mycoprotein product.

2.B.7 Food safety philosophy

This section describes 3F BIO's food safety philosophy. It gives an overview of the key steps that 3F BIO intend to take to ensure that their mycoprotein product is safe to eat and meets all relevant food safety requirements and regulations.

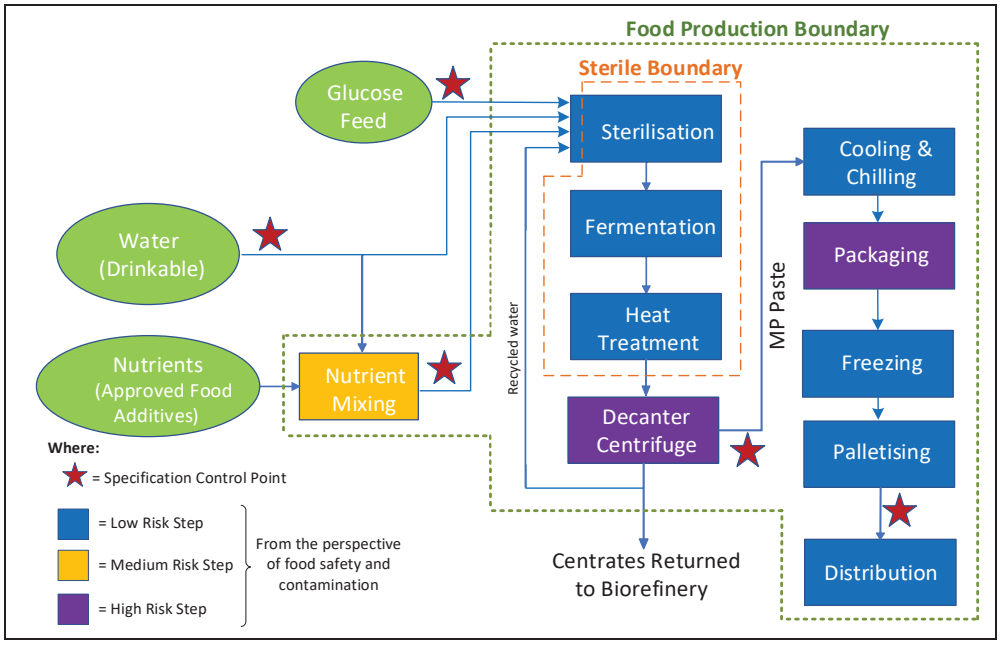

Figure 2. Food production boundary.

Each production step inside the food boundary has been classified as low, medium or high risk with respect to food contamination, following the method set out in BRC Global Standard for Food, issue 8.0.

In general, open handling of food products has been classified as high risk with respect to potential contamination sources, whilst enclosed handling (either within equipment such as a fermenter or within packaging) has been classified as low risk.

The types of potential food contamination that have been considered are as follows:

Table 4. Potential sources of food contamination.

Source of potential food safety issues	Examples
Out of Specification Raw Materials	Mycotoxin Contamination Glucose Heavy Metals Feedstock Pesticides GMOs Contaminated Nutrient Media Contaminated Water Recycled Water
Contamination produced internally to the process (e.g. by the *Fusarium* itself)	Mycotoxin production Ethanol Production Metal fragments
Contamination from the outside environment	Biological Contamination (e.g. contamination of the fermenter with other micro-organisms) Contamination from the outside atmosphere (e.g. dust or bird droppings) Contamination with service fluids or oils Deliberate contamination with foreign materials

Each stream entering the food production boundary will be subject to specification controls. These will be developed according to the philosophies set out in the rest of this section and will be as described in the HACCP studies.

Within the sterile boundary (which encompasses feed sterilisation, fermentation and heat treatment), contamination is prevented by firstly cleaning in place (CIP) and secondly sterilising in place (SIP). After SIP, only sterilised materials are introduced into the fermenter chain, and the fermenter is kept under a positive pressure to maintain sterility.

2.C Composition and Specification of Mycoprotein

By reference to information provided in GRAS No. 91 Notification submitted to the United States Food and Drug Administration (FDA), evidence is provided to demonstrate that the mycoprotein ingredient described in the current notice is substantially equivalent to mycoprotein already on the market.

Analysis of 7 non-consecutive campaigns of ABUNDA mycoprotein demonstrated that the manufacturing process produces consistent products that are in compliance with the established specifications.

'Nutritional value'

3F BIO Ltd has profiled the nutritional content of ABUNDA mycoprotein from a minimum of seven non sequential production runs. All tests were performed in laboratories holding ISO 17025: 2005 certification.

Extensive nutritional profiling has been performed. Results from protein analysis, ash and fibre content are comparable with the literature values reported for the original GRAS. The comparison of typical amino acid composition reported for mycoprotein under GRN No 91. and with those obtained for ABUNDA mycoprotein show small and insignificant differences, with any variance likely to be within the error of the analytical methods employed and will also be the result of a currently small sample population. This data will be expanded upon during additional piloting runs and once commercial production is ongoing. A difference in the total fat is noted between existing mycoprotein and ABUNDA, with ABUNDA mycoprotein having a lower fat content than the existing. This is considered to be a result of the 3F BIO heat treatment regime (see Section 2.B.4) but is not a safety consideration. From the comparison of vitamins and minerals composition some differences are also evident in vitamins B2 and B5 and also in magnesium, manganese and calcium values. It is likely these differences are the result of differing media component concentrations in the production fermenters however these differences are minor and 3F BIO does not consider these significant to the safety or quality of our product.

Table 5. Comparison of typical gross nutritional values reported in GRAS No. 91 with those obtained for ABUNDA® mycoprotein

Nutrients (g/100g dry matter)	Existing Mycoprotein (1) Range	ABUNDA (2)
Crude protein	52-59	54.0
Ash	3-4	3.6
Total fat	12-14	6.2
Total fibre	22-26	28.9
Energy (kcal)	340	390

(1) Sourced from GRAS No. 91
(2) 3FBIO internal data

Table 6. Comparison of typical amino acid composition reported in GRAS No. 91 with those obtained for ABUNDA® mycoprotein

Amino acid (g/100g protein)	Existing Mycoprotein (1) Value	ABUNDA (2)
Alanine	6.3	6.5
Arginine	7.3	6.9
Aspartic acid	10.3	10.4

Glutamic acid	12.5	11.9
Glycine	4.3	4.7
Histidine	3.5	2.5
Isoleucine	5.2	4.9
Leucine	8.5	7.7
Lysine	8.3	7.7
Phenylalanine	4.9	4.7
Proline	4.5	5.0
Serine	5.1	4.9
Threonine	5.5	5.2
Tyrosine	4.0	3.1
Valine	6.2	5.9
Cystein & Cystine	0.8	0.8
Methionine	2.1	2.0
Tryptophan	1.6	1.4

(1) Sourced from GRAS No. 91
(2) 3FBIO internal data

Table 7. Comparison of typical vitamin composition reported in GRAS No. 91 with those obtained for ABUNDA® mycoprotein

Vitamin (g/100g wet weight)	**Existing Mycoprotein [(1)] Value**	**ABUNDA [(2)]**
Thiamine (B1)	0.01	0.02
Riboflavin (B2)	0.23	0.16
Niacin (B3)	0.35	0.38
Pantothenic acid (B5)	0.25	0.18
Biotin	0.02	0.05
Folate	0.01	0.03

(1) Sourced from GRAS No. 91
(2) 3FBIO internal data

Table 8. Comparison of typical mineral composition reported in GRAS No. 91 with those obtained for ABUNDA® mycoprotein

Mineral (mg/100g wet weight)	Existing Mycoprotein [(1)] Value	ABUNDA [(2)]
Calcium	42.5	23.8
Copper	0.5	0.4
Iron	0.5	0.5
Magnesium	45	24.0
Manganese	6.0	1.5
Phosphorus	260	185
Potassium	100	101
Sodium	5.0	5.0
Zinc	9	10.6

[(1)] Sourced from GRAS No. 91
[(2)] 3FBIO internal data

'Metabolism'

The dietary profile of mycoprotein prepared from *F. venenatum* has been extensively discussed[10].

ABUNDA is produced using the same process as that described in the literature, and no significant changes in the metabolism of the product would be expected given that:

- the source organism is the same as that used to manufacture the original product (discussed above),
- the nutritional composition of ABUNDA is substantively the same as that originally produced (Tables 5-8) and the manufacturing process operates on the same principles and parameters.

'Microbiology'

Analysis of 7 non-consecutive campaigns of ABUNDA mycoprotein demonstrated that the microbial quality of the product is in line with the established specifications. Table 9 below presents the internal microbiological criteria of the product.

Table 9. Microbiological quality of mycoprotein

Analysis	Value	Unit
Aerobic Colony Count 72h at 30ºC	< 100	cfu/g
Enterobacteriaceae (presumptive)	< 10	cfu/g

[10] Denny AEA. Mycoprotein and health. Nutrition Bulletin. 2008; 33: 298–310

Coagulase Positive Staphylococci (presumptive)	< 20	cfu/g
E. coli (presumptive)	< 10	cfu/g
Moulds	< 20	cfu/g
Yeasts	< 20	cfu/g
Pseudomonas spp. (presumptive)	< 20	cfu/g
Clostridium perfringens (presumptive)	< 10	cfu/g
Listeria spp. (detection)	Not Detected	In 25g
Salmonella spp. (detection)	Not Detected	In 25g
Sulphite Reducing Clostridia	< 10	cfu/g

'Toxic Elements'

3F BIO has submitted 7 non sequential campaigns of mycoprotein for testing, not only for the presence of known *Fusarium* spp. mycotoxins but also for other mycotoxins of regulatory significance produced by other fungal genera (Aflatoxin B_1, total Aflatoxins and Ochratoxin A).

As shown in Table 2 in section 2.A.2, levels of mycotoxins were not detectable for each of the mycotoxins considered. Table 10 presents the specification limits for mycotoxins in ABUNDA mycoprotein.

Table 10. Specification limits for mycotoxins in mycoprotein

Name of Toxin	**Upper limit in mycoprotein µg/kg (ppb) – as harvested on wet basis**	**LOD [(11)]**
3-Acetyldeoxynivalenol	10	10
15-Acetyldeoxynivalenol	10	10
Deoxynivalenol / Vomitoxin (DON)	10	10
Fumonisin (sum of B1, B2 and B3)	400[12]	10
Fusarenon X (FUSX)	5	5
Nivalenol	5	5
Diacetoxyscirpenol (DAS)	5	5
Neosolaniol (NEO)	10	10
Zearalenone (ZEN)	75[12]	2
HT2 Toxin	2	2

[(11)] Current (2019) lower limit of detection (Synlab Analytics & Services)

[12] The upper limit for Fumonisin (sum of B1, B2 and B3), Zearalenone, Ochratoxin A and Aflatoxins in ABUNDA mycoprotein is based on Commission regulation (EU) No 1881/2006, No 165/2010 and No 594/2012.

T2 Toxin	2	2
Ochratoxin A	3[12]	0.1
Aflatoxin B1	2[12]	0.1
Aflatoxin (sum of B1, B2, G1 and G2)	4[12]	0.1

The specification limits for heavy metals in ABUNDA mycoprotein are shown in Table 11.

Table 11. Specification limits for heavy metals in mycoprotein

Name of heavy metal	Upper limit in mycoprotein mg/kg (ppm) – dry weight	LOD
Arsenic	0.1	< 0.005
Cadmium	0.1	< 0.0004
Lead	0.1	< 0.005
Mercury	0.1	< 0.002

2.C.1 Summary of ABUNDA mycoprotein specification

Definition:

The strict definition of mycoprotein could include the biomass from any fungal source, but in this definition, it means the mycelium of the fungus *Fusarium venenatum*, which has been processed to reduce the level of ribonucleic acids.

Process:

The organism shall be grown axenically on a medium comprising food grade carbohydrate, together with other safe and suitable food grade or reagent grade ingredients using a process described in the "method of manufacture" section. The mycelium shall be processed to reduce the RNA content.

Composition (calculated on a dry weight basis):

a. **Protein** - Not less than 42% calculated as a-amino nitrogen x 6.25
b. Ribonucleic Acid - Not more than 2%;
c. Ash - Not more than 5%;
d. Contaminants:
   i. **Metals** - Lead, arsenic, mercury and cadmium each not more than 0.1 mg/kg (dry weight).
   ii. **Mycotoxins** - Mycoprotein shall not contain mycotoxins in amounts which might constitute a hazard to health. Myco-protein shall be sampled periodically and analysed for representative trichothecenes. Each trichothecene to be less than 20 µg/kg (as is basis).

Nutritional Composition:
Shall be in line with that of mycoprotein product currently in the market.

Microbiological Quality:

Pathogens:	Not detected
Total aerobic count:	≤ 100 cfu/g
Enterobacteriaceae:	< 10 cfu/g
Yeasts and Moulds:	≤ 100 cfu/g
Sulphite Red Clostridia:	< 10 cfu/g
Viable Fusarium:	Not detectable in 1 g

2.D Identification Methods

Fusarium venenatum, as a filamentous fungus, has its cells arranged in the form of filaments (hyphae). This disposition gives mycoprotein (*Fusarium venenatum* biomass) its characteristic meat-like texture.

Mycoprotein's hyphae typically consist on elongated filaments with sparse branching. The mean main hyphal length, meaning the length of the longest hyphae in the mycelium, is typically 400 to 750 µm[13].

Through extensive measurements and analysis, 3F BIO has been able to confirm that their product has equivalent characteristics regarding hyphal length to all previously described in published information about the mycoprotein currently on the market. This is to say that, the mean main hyphal length falls between the reported 400 – 750 µm and no hyperbranched variants have been detected (Figure 3).

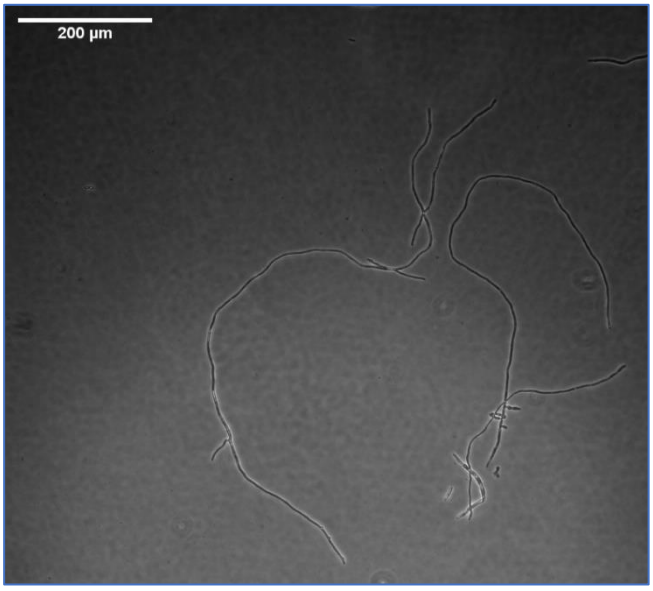

Figure 3: Picture of mycoprotein under phase contrast microscope at 10x magnification.

[13] Finnigan, T.J.A., and Robin Blanchard. 2014. "Edible Fungi."

PART 3. DIETARY EXPOSURE

3.A Mycoprotein quantities in US food

Given that ABUNDA mycoprotein is equivalent to the ingredient that is already in the US market the dietary exposure discussed in the current GRAS notice, is an update of that presented in GRAS No. 91 in 2001. The updated dietary exposure is in accordance with § 170.235 (a). The following section is based on data gathered from products that are marketed under the brand name, Quorn™, to date the only brand to sell foods containing mycoprotein.

According to Euromonitor, the Quorn™ mycoprotein has been exported from Europe to the United States (US) in increasing amounts over the past 6 years, as the US market for meat substitutes has grown. In 2014 2,900 tonnes of the mycoprotein were imported into the US from Europe, and that amount was 11.1 % of the retail frozen meat substitute market (Table 12). In 2019 3,600 tonnes of the mycoprotein were imported into the US from Europe, and that amount was 10.6 % of the retail frozen meat substitute market (Table 12). During those years, the retail value of the mycoprotein exported to the US increased from $7.7 million to $30 million.

Table 12. Data characterizing the export of mycoprotein to the US (Euromonitor, 2019).

Data Type	Unit	2014	2015	2016	2017	2018	2019
Retail Value (Retail Sale Price)	USD million	69.2	79.2	110.8	144.0	214.0	282.9
Total US Frozen Meat Substitute	000 tonnes	26.4	25.2	34.4	30.9	32.9	34.4
Quorn US Retail Market Share	%	11.1	11.7	9.0	9.8	10.5	10.6
Quorn US Retail Volume	000 tonnes	2.9	2.9	3.1	3.0	3.5	3.6
Quorn US Retail Value	USD million	7.7	9.3	10.0	14.1	22.5	30.0

3.B Introduction to the dietary exposure assessment

The National Health and Nutrition Examination Survey (NHANES), “What We Eat In America” (WWEIA) data were used in conjunction with mycoprotein-specific data to estimate the potential dietary exposure to the existing mycoprotein. Reports based on the NHANES data identified the percentage of self-reporting vegetarians in the US population, and characterized the average dietary

consumption of meat, poultry and seafood [14, 15, 16, 17]. The percentage of self-reported vegetarians in the NHANES surveyed population during the years from 2007 through 2010 was 2.1% [16].

3.B.1 Amounts of existing mycoprotein in specific foods

The percentage of mycoprotein content of the Quorn™ meat alternative products on the market in the US was used to estimate the potential average exposure to the mycoprotein in the US diet. There were 15 meatless Quorn™ food items identified on the company website. For each of the 15 products the percentage of mycoprotein was listed, and for 13 products the serving size was specified (Table 13; Quorn™, 2019).

- The serving size for each product was converted to ounces and grams for convenience. The average percent of Quorn™ mycoprotein in the 13 products for which serving sizes were available was 58%.
- The average percent of Quorn™ mycoprotein in all 15 products was 55%.

Data is not available to describe the actual dietary consumption of the Quorn™ mycoprotein. Dietary exposure to the mycoprotein was estimated by multiplying the amount of meat, poultry and seafood consumed daily per person by the percentage of the mycoprotein in the meatless Quorn™ products.

Table 13. Quorn™ Products and percent mycoprotein and serving sizes for each (Quorn™, 2019)

Product Name	% mycoprotein	serving size (g)	Serving size oz.
Meatless breakfast patties	46%	111	3.92
Meatless Gourmet Burgers	37%	80	2.82
Fishless Sticks	12%	100	3.53
Meatless Sharp Cheese Cutlets	37%	110	3.88
Meatless Turkey-Style Deli Slices	65%	64	2.26
Meatless Nuggets	43%	118	4.16
Meatless Meatballs (37%)			
Meatless Roast	60%	113.5	4.00
Meatless Fillets	88%	69	2.43
Meatless Italian Sausages (44%)			

[14] Juan W, Yamini S, Britten P. 2015. Food intake patterns of self-identified vegetarians among the U.S. population, 2007-2010. Procedia Food Science 4; 86-93.

[15] USDA, 2016. A comparison of food patterns equivalents intakes by Americans: What We Eat in America, NHANES 2003-04 and 2011-12. Food Surveys Research Group Dietary Data Brief No 16. September 2016.

[16] USDA, 2017. A comparison of food patterns equivalents intakes by Americans: What We Eat in America, NHANES 2003-04 and 2013-14. Food Surveys Research Group Dietary Data Brief No 17. May 2017.

[17] USDA, 2018. A comparison of food patterns equivalents intakes by Americans: What We Eat in America, NHANES 2003-04 and 2015-16. Food Surveys Research Group Dietary Data Brief No 20. November 2018.

Meatless Pesto & Mozzarella Cutlets	36%	120	4.23
Meatless Buffalo Dippers	53%	105	3.70
Vegan Meatless Pieces	89%	110	3.88
Meatless Grounds	94%	110	3.88
Meatless Steak-Style Strips	91%	110	3.88
Average:	**58%**	**101.58**	**3.11**

3.C NHANES dietary food consumption estimates

The total meat, poultry and seafood consumption from the NHANES WWEIA was identified in publications by the United States Department of Agriculture (USDA) for the years 2003-2004, 2011-2012, 2013-2014 and 2015-2016. The average amount of total meat, poultry and seafood consumed per day by different age groups in the US population is presented in Table 14.

Table 14. Average dietary consumption of meat, poultry and seafood from four NHANES surveys

Total meat, poultry and seafood consumption per day; WWEIA, NHANES. 2003 – 2016				
Age Group (years)	**2003 to 2004 (oz)**	**2011 to 2012 (oz)**	**2013 to 2014 (oz)**	**2015 to 2016 (oz)**
2 to 5	2.5	2.3	2.1	2.3
6 to 11	3.2	3.2	3	3.2
12 to 19	4.3	4.2	4.4	3.9
20+	4.8	4.8	4.9	4.8
All	4.5	4.4	4.5	4.5

The average mycoprotein consumption per day was estimated assuming that the existing mycoprotein products would be consumed in place of meat, poultry and seafood products on a one-for-one basis. To estimate the amount of mycoprotein consumed by eating the meat alternative products, the average meat, poultry and seafood amount consumed per day was multiplied by the average percentage of mycoprotein in the Quorn™ meatless products, 58%. The resulting estimated consumption of mycoprotein is shown in Tables 15 and 16 (reported in ounces and grams).

Table 15. Estimated average dietary consumption of mycoprotein per day, assuming Quorn™ products are substituted in the diet for meat, poultry and seafood (reported in ounces).

Mycoprotein in average total meatless poultry & seafood consumed /person/day (ounces)

(based on WWEIA, NHANES, 2003 - 2016)

Age Group (years)	2003 to 2004 (oz)	2011 to 2012 (oz)	2013 to 2014 (oz)	2015 to 2016 (oz)
2 to 5	1.44	1.33	1.21	1.33
6 to 11	1.85	1.85	1.73	1.85
12 to 19	2.48	2.43	2.54	2.25
20+	2.77	2.77	2.83	2.77
All	2.60	2.54	2.60	2.60

Table 16. Estimated average dietary consumption of mycoprotein per day, assuming Quorn™ products are substituted in the diet for meat, poultry and seafood (reported in grams).

Mycoprotein in average total meatless poultry & seafood consumed/person/day (grams)
(based on WWEIA, NHANES, 2003 - 2016)

Age Group (years)	2003 to 2004 (g)	2011 to 2012 (g)	2013 to 2014 (g)	2015 to 2016 (g)
2 to 5	40.94	37.67	34.39	37.67
6 to 11	52.41	52.41	49.13	52.41
12 to 19	70.42	68.78	72.06	63.87
20+	78.61	78.61	80.25	78.61
All	73.70	72.06	73.70	73.70

3.D Dietary mycoprotein consumption level - conclusion

For all age group populations, the average Quorn™ mycoprotein consumed in one day is estimated to be between 2.5 to 2.6 ounces or 72 to 74 grams wet weight (equivalent to 0.30 g dry weight/kg/day). It is likely that only a minority of the US population consumes meat alternatives on a regular basis, given that the NHANES survey identified only 2.1% of the population as self-reported vegetarians[16]. The estimated dietary consumption of Quorn™ mycoprotein is expected to apply primarily to a sub-population of consumers that eat meat alternatives rather than meat, poultry and seafood.

In GRAS notice GRN No.91 the EDI is based on data from products that are currently on the market and this updated value of 0.30 g dry weight/kg/day sits within the previously defined range. This previous data defining EDI for mycoprotein ranged from 0.01 - 0.18g dry weight/kg/day for the general US population and 0.24 - 0.46g dry weight/kg/day for the meat avoider vegetarian population)

As such no change in EDI is seen based on all data available.

PART 4. SELF-LIMITING LEVELS OF USE

No known self-limiting levels of use are associated with the mycoprotein ingredient.

PART 5. HISTORY OF CONSUMPTION OF THE SUBSTANCE FOR FOOD USE BY A SIGNIFICANT NUMBER OF CONSUMERS (OR ANIMALS IN THE CASE OF ANIMAL FOOD) PRIOR TO JANUARY 1, 1958

Not applicable.

PART 6. BASIS FOR THE CONCLUSION OF GRAS STATUS

6.A. Current Regulatory Status

In 2001, the FDA has issued a 'no question' letter for mycoprotein currently on the market – GRAS notice No. 91. In this GRAS notice, toxicity studies on mycoprotein were presented supporting the safety of use of mycoprotein as a food ingredient. The FDA did not question the acceptability and suitability of these studies to establish the safety of mycoprotein for the proposed food uses.

The FDA also had no questions on the summary of safety, concluding that mycoprotein use in a variety of products excluding meat, poultry and infant formula is safe.

6.B Intended use

3F BIO is intending to sell their mycoprotein product on a B2B basis for it to be used in a variety of meals – excluding meat, poultry and infant formula.

6.C Review of safety data

As noted above, the FDA raised no questions to the original GRAS notice for mycoprotein (GRN No. 91) regarding their conclusion that mycoprotein is GRAS under the intended conditions of use, provided that neither trichothecene mycotoxins (represented by nivalenol, deoxynivalenol, 3-acetyldeoxynivalenol, diacetoxyscirpenol, fusarenone X, and neosolaniol) nor fusarin mycotoxins were detectable in the ingredient.

The specification for ABUNDA mycoprotein in this notice is equivalent to those described in the previous notice, and on this basis it is proposed that the composition, safety data, and other pertinent information discussed in GRN No. 91 are also applicable to the safety of ABUNDA mycoprotein in this GRAS notice. The information is hereby incorporated by reference to these documents.

However, due to the fact the GRN No. 91 was submitted in 2001, 3F BIO has conducted a review focusing on literature that has been published since last submission, specifically papers published between January 2002 and September 2019[18]. Since GRAS No. 91 submission,

- five papers were identified discussing nutrition and satiety [19, 20, 21, 22, 23]
- six papers were identified related to adverse reactions, hypersensitivity and intolerances after consuming mycoprotein [24,25,26,27,28,29];
- seven papers (including a dose response study, a randomised controlled trial and a pilot study) were focusing on glycemia/insulinemia, blood lipids and fibre [21, 23, 30, 31, 32, 33, 34].

A general conclusion, in line with the previous GRAS notice, is that mycoprotein is a good source of protein and it has a long and established history of use across multiple markets, and which can be assumed to represent a wide range of consumer age and demographic profiles.

The review of the literature also supports the conclusion previously confirmed that whilst there is a potential for any source of protein to create an allergic response for some consumers, the level of incidence of this for mycoprotein is very low and is notably lower than the food allergens that are recognised in either the US or the EU.

[18] 3F BIO internal document: Review of mycoprotein studies: 2002 – 2019, Ref. QM03-D-003
[19] Derbyshire and Ayoob; Mycoprotein: Nutritional and Health Properties. Nutrition Today. 2018; 54(1):7-15
[20] Bottin J, Cropp E, Finnigan T, Hogben A. Mycoprotein reduces energy intake and improves insulin sensitivity compared to chicken. Obes Facts. 2012; 5(1):55-79.
[21] Bottin J H. Nutritional and surgical influences on appetite regulation and body composition in overweight and obese humans. Thesis submitted for the degree of Doctor of Philosophy from Imperial College London (2014).
[22] Bottin JH, Swann JR, Cropp E. Mycoprotein reduces energy intake and postprandial insulin release without altering glucagonlike peptide-1 and peptide tyrosine-tyrosine concentrations in healthy overweight and obese adults: a randomised-controlled trial. British Journal of Nutrition. 2016; 116(2): 360-374.
[23] Williamson D, Geiselman P, Lovejoy J, Greenway F, Volaufova J, Martin C K, Arnett C, Ortego L. Effects of consuming mycoprotein, tofu or chicken upon subsequent eating behaviour, hunger and safety. Appetite 46. 2006; 41–48.
[24] Katona S J, Kaminski E R. Sensitivity to Quorn mycoprotein (Fusarium venenatum) in a mould allergic patient. Journal of Clinical Pathology. 2002; 55: 876-879.
[25] Hoff M, Trueb RM, Ballmer-Weber BK, Vieths S, Wuethrich B. Immediate-type hypersensitivity reaction to ingestion of mycoprotein (Quorn) in a patient allergic to molds caused by acidic ribosomal protein P2. The Journal of Allergy and Clinical Immunology. 2003; 111(5): 1106-10.
[26] Van Durme P, Ceuppens JL, Cadot P. Allergy to ingested mycoprotein in a patient with mold spore inhalant allergy. Journal of Allergy and Clinical Immunology. 2003; 112: 452-4.
[27] Dzeladini L, Chan D, Kummerow M. A case report of mycoprotein allergy. Internal Medicine Journal. 2017; 47 (Suppl 5): 5-33.
[28] Jacobson M F, DePorter J. Self-reported adverse reactions associated with mycoprotein (Quorn-brand) containing foods. Annals of Allergy, Asthma & Immunology. 2018; 120: 626-630.
[29] Finnigan T JA, Wall B T, Wilde P J, Stephens F B, Taylor S L, Freedman M R. Mycoprotein: The Future of Nutritious Nonmeat Protein, a Symposium Review. Current Developments in Nutrition. 2019; 3 (Issue 6).
[30] Bottin J, Cropp E, Ford H, Betremieux L, Finnigan T JA, Frost G. Mycoprotein reduces insulinemia and improves insulin sensitivity Proceedings of the Nutrition Society. 2011; 70 (OCE6), E372.
[31] Dunlop MV, Kilroe SP, Bowtell JL, Finnigan T JA. Mycoprotein represents a bioavailable and insulinotropic non-animal derived dietary protein source: a dose response study. British Journal of Nutrition. 2017; 118: 673-85.
[32] Denny AEA. Mycoprotein and health. Nutrition Bulletin. 2008; 33: 298–310
[33] Ruxton C HS, McMillan B. The impact of mycoprotein on blood cholesterol levels: a pilot study. British Food Journal. 2012; 112 (10): 1092-1101
[34] Finnigan T JA, Wall B T, Wilde P J, Stephens F B, Taylor S L, Freedman M R. Mycoprotein: The Future of Nutritious Nonmeat Protein, a Symposium Review. Current Developments in Nutrition. 2019; 3 (Issue 6)

6.C.1 Intolerance and fibre content

Mycoprotein's nutritional composition and its original structure were the basis of research projects investigating the effect of mycoprotein on health in humans.

With billions of mycoprotein based products consumed over a 30+ year period in numerous countries around the world, there are very few cases of published intolerance (four cases identified in the literature since 2002). Of the four individual case reports, all suggest that patients who are allergic to mould might react adversely to mycoprotein due to cross-reactivity [24, 25, 26, 27].

All protein sources have a potential level of intolerance or allergenicity and at the level reported, mycoprotein demonstrates an extremely low risk.

One of the above case reports aimed to identify and characterise the potential allergen that was responsible for a reaction of an asthmatic male patient who ingested mycoprotein [25]. Through a double-blind placebo-controlled oral challenge the authors concluded that the allergic reaction was not due to a primary sensitization, but due to cross-reactivity with aero-allergens. The patient's reaction to mycoprotein was most likely the result of cross-reactivity between mycoprotein derived from *Fusarium venenatum* and the 60S acidic ribosomal protein P2, which was identified as allergen Fus c 1 from *Fusarium culmorum* and that was also described as allergen for the moulds *C. herbarum*, *A. fumigatus*, and *A. alternate.*

The mycoprotein manufacturer's database indicate that 92% of reported illnesses are associated with GI symptoms[34]. In 2011 an expert panel was convened to review adverse reactions related to mycoprotein and potential causes. This comprised scientists from US, UK and Australia.

The conclusions of the panel state that gastrointestinal (GI) symptoms were likely to be related to the high fibre content of mycoprotein. The panel hypothesised that in certain individuals or under certain conditions, consuming mycoprotein could speed up the normal transit of foods from the small to the large intestine. This could, in turn, cause the fibre in mycoprotein to be fermented very rapidly in the large intestine, leading to symptoms of gastrointestinal distress of the type reported by some consumers. Those at risk from this type of gut response may have an imbalance in their normal gut bacteria, an unusual dietary intake of fibre (too low or too high) or may suffer from irritable bowel syndrome[35].

In 2015, the York Health Economics Consortium conducted a systematic review of allergic reactions to mycoprotein[36]. Among 30 experimental studies, only two reactions were confirmed. The consortium concluded that reported intolerance reactions to mycoprotein are very low relative to other common allergenic foods, however rare cases of true allergy to mycoprotein do occur, as for many common foods, e.g. wheat, eggs and potatoes.

6.C.2 Safety studies

No animal toxicity studies, or human clinical studies, were conducted by 3F BIO for the purposes of this GRAS notice. All the safety data in support of this notice are based on the existing evaluation described by the previous notifier that supports the conclusion that the proposed uses would not be expected to produce any acute or chronic adverse effects. Therefore, the current evaluation of all available analytical, animal and human safety data, as well as market information on typical levels

[35] York Health Economics Consortium (YHES, 2015), https://www.mycoprotein.org/faqs

and frequency of consumption of mycoprotein, leads to the conclusion that the proposed intended use of the ingredient will not be expected to produce any acute or chronic adverse effects in individuals consuming these food products under the intended conditions of use.

6.C.2.1 Animal toxicity studies reviewed in previous GRAS notice

GRN No. 91 describes a variety of in vitro, acute, sub-chronic, and chronic studies that the previous notifier conducted to verify the safety of mycoprotein. All the data from the above-mentioned studies support the safety of mycoprotein.

6.C.2.2 Human studies reviewed in previous GRAS notice

GRN No. 91 reported that four studies were performed to assess human tolerance to mycoprotein. Mycoprotein, with levels ranging from 10 to 40 g/day, was fed to human volunteers for periods ranging from 1 to 30 days. Subjects who recorded adverse responses were re-challenged under controlled conditions. The reported events did not recur in any of the cases, except those in which the subject was shown to be atopic to fungus-derived foods. The results indicated that mycoprotein is well tolerated by humans and has extremely low allergenic potential (extract from GRAS No. 91, *also supported by the findings in 3F BIO mycoprotein report – 2002 to 2019*). A significant history of use in Europe has also demonstrated that humans tolerate mycoprotein. Finally, mycoprotein has been consumed by US population for the past 19 years and no significant numbers of reported incidences.

6.C.3 Safety of production organism

The non-GMO production organism utilised in the manufacture of ABUNDA mycoprotein is not mutagenic, genotoxic, or toxic.

6.D Safety Determination

A number of human and animal studies have reported benefits of mycoprotein with no major adverse effects. There is broad-based and widely disseminated knowledge concerning the chemistry of mycoprotein.

ABUNDA mycoprotein is manufactured under GMP using common food industry materials and processes. 3F BIO Ltd uses a HACCP-controlled manufacturing process and rigorously tests its final production batches to verify adherence to quality control specifications. This GRAS determination is based on the data and information generally available and consented opinion about the safety of ABUNDA mycoprotein.

The following safety evaluation fully considers the composition, intake, and nutritional, microbiological, and toxicological properties of ABUNDA mycoprotein as well as appropriate corroborative data.

1. Analytical data from 7 non sequential production campaigns indicate that ABUNDA complies reliably with the established food-grade product specifications and meets all applicable specification standards.
2. The intended use it the same as that described in GRN No. 91.

3. In the previous GRAS notice (GRN No. 91) to the FDA, the safety of mycoprotein has been established in animal toxicity studies (in vitro, acute, sub-chronic, and chronic studies) and is further supported by human clinical studies.

6.E. Conclusions and General Recognition of the Safety of ABUNDA mycoprotein

GRAS status confirmed via scientific procedures is based on generally available and accepted scientific data, information, methods, or principles, which ordinarily are published and may be verified by unpublished scientific data, information, or methods.

6.E.1. Common Knowledge Element of the GRAS Determination

Mycoprotein has been safely used as a food ingredient around the world for over three decades. As a result, a number of comprehensive reviews of the safety and nutritional benefits of mycoprotein have been published.

Numerous human and animal studies have reported no major adverse effects caused by mycoprotein already on the market.

The literature indicates that mycoprotein currently on the market is a good source of protein and it has a long and established history of use across multiple geographies, which is assumed to represent a wide range of consumer age and demographic profiles.

In addition, the FDA had no question on GRAS notice No. 91 relating to the safety of mycoprotein (GRN No. 91, 2001).

6.E.2. Technical Element of the GRAS Determination (Safety Determination)

3F BIO Ltd uses a HACCP-controlled manufacturing process for ABUNDA mycoprotein and rigorously tests its final production batches to verify adherence to quality control specifications and, thus, are manufactured consistent with GMP for food (21 CFR Part 110 and Part 117 Subpart B). The raw materials and nutrients used in the manufacturing process are food grade and/or commonly used in fermentation and food manufacturing processes.

The intended use of ABUNDA mycoprotein is the same as that from the previous GRAS, which have been determined to be safe through scientific procedures as set forth in 21 CFR 170.3(b); thus, satisfying the “technical” element of the GRAS determination.

We concluded that ABUNDA mycoprotein, produced using a non-GMO production microorganism, *Fusarium venenatum*, is GRAS based on scientific procedures. The proposed use of ABUNDA mycoprotein is safe within the terms of the Federal Food, Drug, and Cosmetic Act (meeting the standard of reasonable certainty of no harm).

We are not aware of any information that would be inconsistent with the finding that the proposed use of ABUNDA mycoprotein, meeting appropriate specifications, is GRAS. Recent reviews of the scientific literature revealed no material adverse health concerns.

6.F. Discussion of Information Inconsistent with GRAS Determination

We are not aware of information that would be considered inconsistent with the finding that the proposed use of ABUNDA mycoprotein preparation in foods meeting appropriate specifications is GRAS.

PART 7. DATA AND INFORMATION ARE GENERALLY AVAILABLE

7.A. Data and Information that are generally available

Bottin J H. Nutritional and surgical influences on appetite regulation and body composition in overweight and obese humans. Thesis submitted for the degree of Doctor of Philosophy from Imperial College London (2014).

Bottin J, Cropp E, Finnigan T, Hogben A. Mycoprotein reduces energy intake and improves insulin sensitivity compared to chicken. Obes Facts. 2012; 5(1):55-79.

Bottin J, Cropp E, Ford H, Betremieux L, Finnigan T JA, Frost G. Mycoprotein reduces insulinemia and improves insulin sensitivity Proceedings of the Nutrition Society. 2011; 70 (OCE6), E372.

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Dunlop MV, Kilroe SP, Bowtell JL, Finnigan T JA. Mycoprotein represents a bioavailable and insulinotropic non-animal derived dietary protein source: a dose response study. British Journal of Nutrition. 2017; 118: 673-85.

Dzeladini L, Chan D, Kummerow M. A case report of mycoprotein allergy. Internal Medicine Journal. 2017; 47 (Suppl 5): 5-33.

Finnigan T JA, Wall B T, Wilde P J, Stephens F B, Taylor S L, Freedman M R. Mycoprotein: The Future of Nutritious Nonmeat Protein, a Symposium Review. Current Developments in Nutrition. 2019; 3 (Issue 6).

Finnigan, T.J.A., and Robin Blanchard. 2014. “Edible Fungi.”

GRAS No. 91. https://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices&id=91

Hoff M, Trueb RM, Ballmer-Weber BK, Vieths S, Wuethrich B. Immediate-type hypersensitivity reaction to ingestion of mycoprotein (Quorn) in a patient allergic to molds caused by acidic ribosomal protein P2. The Journal of Allergy and Clinical Immunology. 2003; 111(5): 1106-10.

Jacobson M F, DePorter J. Self-reported adverse reactions associated with mycoprotein (Quorn-brand) containing foods. Annals of Allergy, Asthma & Immunology. 2018; 120: 626-630.

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Ruxton C HS, McMillan B. The impact of mycoprotein on blood cholesterol levels: a pilot study. British Food Journal. 2012; 112 (10): 1092-1101

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Van Durme P, Ceuppens JL, Cadot P. Allergy to ingested mycoprotein in a patient with mold spore inhalant allergy. Journal of Allergy and Clinical Immunology. 2003; 112: 452-4.

Williamson D, Geiselman P, Lovejoy J, Greenway F, Volaufova J, Martin C K, Arnett C, Ortego L. Effects of consuming mycoprotein, tofu or chicken upon subsequent eating behaviour, hunger and safety. Appetite 46. 2006; 41–48.

YHES, 2015, https://www.crd.york.ac.uk/PROSPEROFILES/10132_PROTOCOL_20140509.pdf

Yoder W.T. and Christianson L.M. 1998. Species-Specific Primers Resolve Members of Fusarium Section Fusarium. Taxonomic Status of the Edible ''Quorn'' Fungus Re-evaluated. Fungal Genetics and Biology, 23, 68-80.

https://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/gout-diet/art-20048524

http://www.ukgoutsociety.org/docs/goutsociety-allaboutgoutanddiet-0113.pdf

https://nrrl.ncaur.usda.gov/

https://www.mycoprotein.org/faqs

7.B. Data and information that are not generally available

The following data and information, relevant to the safety of the intended uses of ABUNDA mycoprotein and discussed in Part 6 of this report, are not generally available:

Appendix A – 3F BIO internal document: Review of mycoprotein studies: 2002 – 2019, Ref. QM03-D-003.

Appendix B – 3FBIO internal document: Product description and intended use, FS02-D-001.

Appendix C – Example laboratory reports (including toxic elements, amino acids, vitamins, microbiology, basic nutritional).

APPENDIX A

3F BIO internal document: Review of mycoprotein studies: 2002 – 2019, Ref. QM03-D-003

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Executive Summary & Conclusions

3F BIO Ltd is developing technology which adapts the downstream process for producing mycoprotein creating an integrated zero waste process and improving the overall economics, but which maintains the core aspects of the legacy fermentation process and within which it also maintains the same strain and feedstock as used in the legacy process detailed in the GRAS notice submitted to the US FDA under GRN No. 91.

3F BIO Ltd wishes to work collaboratively and proactively with the US FDA in order to reaffirm the regulatory approval for product produced using this process, and constructive discussions are in progress. This report has been compiled in response to a request from the FDA for a review of clinical studies supporting continued safe use and consumption of mycoprotein since the GRAS notice in 2001, with the view to supporting a successful launch of ABUNDA mycoprotein into the market in 2021.

This report summarises the findings of a literature review conducted by 3F BIO to collate information regarding recent mycoprotein studies, reports, trials and scientific opinions related to both food safety and nutritional benefits. This review has looked at studies and other relevant scientific papers dated from 2002 to 2019 which relate to mycoprotein and food safety, its health and nutritional impacts/benefits.

A general conclusion is that mycoprotein is a good source of protein and it has a long and established history of use across multiple markets, and which is assumed to represent a wide range of consumer age and demographic profiles. The report also supports the conclusion previously confirmed that whilst there is a potential for any source of protein to create an allergic response for some consumers the level of incidence of this for mycoprotein is very low and is notably lower than the recognised food allergens that are recognised in either the US or the EU.

The reported incidents of genuine substantiated allergic or intolerant response show 5 incidents over the last 20+ years and which compares to reported sales of more than 5 billion consumer packs.

There is a recognised risk that for some consumers there is a greater risk of some form of intolerance, and this can also be common for all sources of proteins, where as an example the level of intolerance to wheat protein may be as high as 1:8 on representing more than 12-15% of the population. In the case of mycoprotein, specifically produced with Fusarium venenatum, a systematic review of the evidence indicates that the incidence of intolerance to mycoprotein remains exceptionally low (between 1 in 100,000 and 200,000). Very few cases of confirmed intolerance have been documented and, where provided, data suggests a complex interaction of factors and not a clearly attributable route cause of mycoprotein. Scientists that have conducted mycoprotein studies focusing on its nutritional, health, and environmental benefits all confirmed its safety and its role in a healthy diet.

Regarding positive nutritional claims, a recent study has shown that mycoprotein is a bioavailable source of protein that is also insulinotropic i.e. meaning that it stimulates the production and/or activity of insulin. Further studies are needed but this indicates that mycoprotein may help to stimulate muscle protein synthesis rates. Another conclusion from the current review is that when mycoprotein is consumed as part of a healthy diet, it has potential satiety effects and appetite regulation. The studies reviewed also suggest that mycoprotein could improve cholesterol and low-density lipoprotein profiles, particularly for those with elevated baseline blood cholesterol levels.

Furthermore, high levels of mycoprotein significantly reduce energy intake in healthy overweight adults. Mycoprotein might be useful in the dietetic prevention of body weight gain. Further research is required on long term studies to investigate the potential of mycoprotein in the prevention of obesity and type 2 diabetes melitus.

This scientific research is additive to 30+ years of mycoprotein where the level of adverse reactions is incredibly low. They underline the potential for mycoprotein, now not solely under the control of a single company, to form part of a more sustainable and healthy protein source.

For the overwhelming majority of individuals, mycoprotein represents a safe foodstuff.

Section 1: Introduction

Background

Mycoprotein is a food ingredient derived from a filamentous micro-organism, Fusarium venenatum. It is produced by a continuous, axenic fermentation process, using a food grade carbohydrate substrate. The organism is unchanged from its natural state and has not been subject to any form of genetic manipulation. Mycoprotein is manufactured to a rigorous and demanding specification, with strict process controls and quality assurance systems in place. No consignment of mycoprotein is released for use in food products unless representative samples have been analysed to demonstrate absence of mycotoxins.

Mycoprotein is rich in high quality protein, with a high dietary fibre content, a low level of available carbohydrates and the lipids present are primarily polyunsaturated fatty acids. Because of its filamentous nature it has a natural texture which makes it ideal for the creation of a wide range of food items that can form meal centres as alternatives to meat, co-products with meat, or that offer particular characteristics to other types of foods. Conventional cooking methods are used, and, in this respect, products based on mycoprotein are no different from other food products.

Mycoprotein products have been on sale in the United Kingdom since January 1985; sales in other European countries began in 1991; sales in the US commenced in 2000 and subsequently in Australia, South Africa and some Asian markets in the last decade

An estimated 5 billion servings of products containing mycoprotein have been consumed worldwide since launch (Finnigan et al., 2019) and to date the significant majority of products sold have been under the brand name Quorn™, with a small percentage sold under private label / retailer brand.

3F BIO philosophy

With demand for protein increasing at 3 times the rate of expected population growth and demand for meat alternatives growing by over 5 times that of protein, traditional farming is not a sustainable solution to meet future protein demands as a sole solution. 3F BIO believes that technology and specifically biotechnology support a more efficient use of scarce natural resources and enable a more sustainable solution to the future of protein.

3F BIO Ltd have developed and validated a process to transform the cost economics of mycoprotein supply capacity and to enable an increased level of overall global capacity, with the intention to install supply capacity local to regional markets.

Macro forecasts from the FAO and other experts predict that in order to avoid the negative environmental impacts of conventional livestock farming and to align with changes in consumer preference, the demand for non-livestock protein may increase by >100M tonnes in the next 10 years (source: World Bank, United Nations, AT Kearney, 2019). Fermentation processes are increasingly recognised as being an advantaged solution to meet this demand, producing high scale high quality protein and are complimentary to existing farming and agricultural processes. The conversion of the starch sources within grains such as wheat and maize into food grade protein enables a solution for future food demand which can be locally sourced, and which has significantly lower impacts in the environment.

3F BIO's process to produce mycoprotein retains the core elements of the legacy production process, utilising the same stain, the same feedstock and the same quality principles. This produces a product which has been demonstrated to be functionally, nutritionally, physically and chemically equivalent to the legacy production process. 3F BIO's process has an additional cost and environmental benefit based on its 'zero-waste' process that is achieved by integrating any waste from the fermentation process into a bioethanol refinery. This reduces the overall cost by avoiding the processing costs of unfermented 'waste' sugars and proteins which can be valorised within the existing infrastructure and fully separate process that produces bioethanol. In addition to lower operating costs, this solution also creates a more efficient capital solution and is complimentary to the aims of the biorefinery operators who are seeking to diversify and optimise their capacity.

3F BIO development timescale

Building on research from within the University of Strathclyde in Scotland and a patent that was filed in 2014, 3F BIO was founded in 2015. The process for producing mycoprotein has been demonstrated at lab and food grade pilot scale, with controlled production of mycoprotein at various scales from 10L, 150L and ultimately 15,000L. The 15,000L scale production represents a 1/10 scale of the planned industrial scale operation and has been conducted with representative materials and hygiene procedures.

The initial food grade production was completed in accordance with 3F BIO's technical data specification using the capacity and facilities from a shared access contract manufacturing organisation based in Ghent, Belgium. The initial validated food grade production run took place in August 2018, and since then there have been 7 successful pilot production runs. The analysis from each run (nutritional, chemical and physical) confirms the product's consistency and is also comparable to the existing mycoprotein specification.

This supports the equivalence to the legacy published specification for mycoprotein, including the specification detailed in the GRAS notice submitted to the US FDA under GRN No.91 in 2001.

Prototypes for product formats including meat alternatives, meat hybrids, noodles, petfood and dairy alternatives have been developed by working with internationally recognised consumer goods companies and this has validated market interest and demand for the product from prospective customers both in Europe and the US. This leads 3F BIO to the position as at October 2019 where it has initiated a capital project to install its first industrial scale plant which is targeted to be operational in mid-2021.

In October 2019, 3F BIO initiated a project working with 9 industrial partners to build and operate a first of its kind integrated facility to produce food grade protein from renewable resources. This project has support from the EU's Bio Based Industries Joint Undertaking (BBI-JU) and supports the EU's aim to achieve protein security. To be able to respond to anticipated customer demand, 3F BIO also plans to develop a similar solution for local production in North America and will progress this based on a target timescale to initiate construction in the period from 2021 to 2023. At this stage the location and partner for this is not confirmed.

Section 2: Objectives & Methods

This report has been compiled in response to a request by the FDA for a review of clinical studies supporting continued safe use and consumption of mycoprotein since the GRAS notice in 2001, with the view to supporting a successful launch of ABUNDA mycoprotein into the market in 2021.

The report summarises the findings of a literature review assessing mycoprotein studies, reports, trials and scientific opinions related to both food safety and nutritional benefits or mycoprotein. The report cannot claim to be exhaustive, but shows all data sources that were found or identified as being publicly available by 3F BIO.

Mycoprotein's nutritional composition and its original structure were the basis of research projects investigating the effect of mycoprotein on health in humans (Derbyshire and Ayoob, 2018). Mycoprotein has a favourable fatty acid profile (being relatively low in saturates), a fibre content that is comparable with other vegetarian protein sources, and a naturally low sodium content. Mycoprotein is a good source of zinc and selenium but the levels of iron and vitamin B12 in mycoprotein are low in comparison to red meat. A small number of human studies investigated the effects of mycoprotein on cholesterol reduction, satiety and insulinemia/glycemia. These studies have shown beneficial effects of mycoprotein compared with meat on blood lipid profiles (Turnbull et al., 1992, Ruxton and McMillan, 2010), glucose homeostasis (Turnbull and Ward, 1995, Denny et al., 2008) and appetite (Williamson et al., 2006).

The scientific papers identified during this literature search are categorised in 4 main groups:

Group A: Intolerance

2002, Sensitivity to Quorn mycoprotein (Fusarium venenatum) in a mould allergic patient.

2003, Immediate-type hypersensitivity reaction to ingestion of mycoprotein (Quorn) in a patient allergic to moulds caused by acid ribosomal protein P2.

2003, Allergy to ingested mycoprotein in a patient with mould spore inhalant allergy.

2017, A case report of mycoprotein allergy.

2018, Self-reported adverse reactions associated with mycoprotein (Quorn-brand) containing foods.

2018, Mycoprotein: The Future of Nutritious Nonmeat protein, a Symposium Review.

Group B: Glycemia/Insulinemia

2011, Mycoprotein reduces insulinemia and improves insulin sensitivity.

2012, Mycoprotein reduces energy intake and improves insulin sensitivity compared to chicken.

2016, Mycoprotein reduces energy intake and postprandial insulin release without altering glucagonlike peptide-1 and peptide tyrosine-tyrosine concentrations in healthy overweight and obese adults: a randomised-controlled trial.

2017, Mycoprotein represents a bioavailable and insulinotropic non-animal-derived dietary protein source: a dose-response study.

Group C: Blood Lipids

2008, Mycoprotein and health.

2010, The impact of mycoprotein on blood cholesterol levels: a pilot study.

2018, Mycoprotein: The Future of Nutritious Nonmeat protein, a Symposium Review.

Group D: Nutrition and Satiety

2006, Effects of consuming mycoprotein, tofu or chicken upon subsequent eating behaviour, hunger and safety.

2012, Mycoprotein reduces energy intake and improves insulin sensitivity compared to chicken.

2014, Nutritional and surgical influences on appetite regulation and body composition in overweight and obese humans.

2016, Mycoprotein reduces energy intake and postprandial insulin release without altering glucagonlike peptide-1 and peptide tyrosine-tyrosine concentrations in healthy overweight and obese adults: a randomised-controlled trial.

2018, Mycoprotein – Nutritional and Health Properties.

Section 3: Results

Group A results: Intolerance data

With billions of mycoprotein based products consumed over a 30+ year period in numerous countries around the world, there are only a few cases of published intolerance (5 cases since 2002). All protein sources have a potential level of intolerance or allergenicity and at the level reported, mycoprotein demonstrates an extremely low risk. Of the 5 individual case reports, all suggest that patients who are allergic to mould might react adversely to mycoprotein due to cross-reactivity (Katona and Kaminski, 2002, Van Durme P et al., 2003, Hoff et al., 2003, Dzeladini et al., 2017).

One of the above case reports aimed to identify and characterise the potential allergen that was responsible for a reaction of an asthmatic male patient who ingested mycoprotein (Hoff et al, 2003). Through a double-blind placebo-controlled oral challenge the authors concluded that the allergic reaction was not due to a primary sensitization, but due to cross-reactivity with aero-allergens. The patient's reaction to mycoprotein was most likely the result of cross-reactivity between mycoprotein derived from Fusarium venenatum and the 60S acidic ribosomal protein P2, which was identified as allergen Fus c 1 from Fusarium culmorum and that was also described as allergen for the moulds C. herbarum, A. fumigatus, and A. alternate.

Adverse reactions of people consuming mycoprotein are not always confirmed to be caused by this ingredient as other allergens were consumed in the same day by the person with the reaction. The UK's Food Standards Agency (FSA) states that "research estimates that between 1 in 100,000 to 200,000 people may react to it". All protein foods have the potential to cause an adverse reaction in some consumers. About one in 200 people are thought to be intolerant to soya for example (https://www.mycoprotein.org/faqs).

The mycoprotein manufacturer's database indicate that 92% of reported illnesses are only associated with GI symptoms (Finnigan et al., 2019).

In 2011 an expert panel was convened to review adverse reactions related to mycoprotein and potential causes. This comprised scientists from US, UK and Australia. The conclusions of the panel state that GI symptoms were likely to be related to the high fibre content of mycoprotein. The panel hypothesised that in certain individuals or under certain conditions, consuming mycoprotein could speed up the normal transit of foods from the small to the large intestine. This could, in turn, cause the fibre in mycoprotein to be fermented very rapidly in the large intestine, leading to symptoms of gastrointestinal distress of the type reported by some consumers. Those at risk from this type of gut response may have an imbalance in their normal gut bacteria, an unusual dietary intake of fibre (too low or too high) or may suffer from irritable bowel syndrome (YHES, 2015, https://www.mycoprotein.org/faqs).

In 2015, the York Health Economics Consortium conducted a systematic review of allergic reactions to mycoprotein (Finnigan et al.,2019). Among 30 experimental studies, only two reactions were confirmed. The consortium concluded that reported intolerance reactions to mycoprotein are very low relative to other common allergenic foods, however rare cases of true allergy to mycoprotein do occur, as for many common foods, e.g. wheat, eggs and potatoes.

The Centre for Science in the Public Interest (CSPI) has collected anecdotal reports on adverse reactions to mycoprotein, both GI complaints and allergic reactions, through its website. All reports analysed in this study were self-reports and not confirmed by oral food challenges. The symptoms

attributed to mycoprotein could have been caused by other foods, drugs or other agents. In addition, some of the consumers of the self-reports analysed in this paper could have filed fictious negative reviews because of factors other than medical reasons, such as possible lack of refund, customer service dissatisfaction and others (Jacobson and DePorter, 2018).

During a symposium reviewing mycoprotein (Finnigan et al., 2019) it was noted that ingestion of any novel dietary protein, including mycoprotein, may elicit an allergic reaction. One of the speakers explained that the manufacturer of mycoprotein has tracked worldwide consumer complaints since mycoprotein entered the UK market in 1985. Examination of all reported adverse reaction complaints indicates that the incidence of worldwide adverse reactions to the company over > 30 years remains extremely low (over 15 years period the frequency or reported illnesses (RI) per packages sold was 1 RI per 683,665 packages). The Symposium review discussed the results of the CSPI claims and note that CSPI have failed to present the denominator that would allow for an estimate of the frequency of the unsafe reactions. The authors also suggest that self-reported data should be treated with caution. The authors noted that novel food sources of protein introduced in the US food supply (such as lupine, canola protein isolate, insects, wheat protein isolate) can become allergenic, but from an allergy perspective, mycoprotein may be among the safest novel protein sources on the market.

Anaphylaxis.org.uk suggests to always read the ingredient list of a product, especially when the consumer has a confirmed allergy to common foods. They recommend that people who suspect they may have suffered symptoms suspected to have been triggered by a mycoprotein product to see their GP. The GP may refer them to an allergy clinic where a skin prick test or blood tests can be performed as part of the diagnosis. It may not be an allergy. Anphylaxis.org.uk also explains that people that may react to mycoprotein also suffer from symptoms when they are exposed to mould spores. They also explain that this happens due to a process called cross-reactivity, where the proteins in one food or substance share potential allergenic characteristics with those in another food or substance. They advise that if a person is sensitised to mould, it is important to remember that it can be formed anywhere, from window frames to decaying foods.

Group B results: Glycemia and Insulinemia

From the studies reviewed, the evidence suggests that mycoprotein may have a positive effect on control of blood glucose levels. In 2011, Bottin et al., assessed whether the consumption of an average serving of mycoprotein would lower post prandial levels of glucose and insulin and improve insulin resistance. The study demonstrated a significant reduction in insulin levels following consumption of mycoprotein compared to whey protein. Mycoprotein significantly improved post prandial insulin resistance. These results confirmed that mycoprotein could play a role in glucose homeostasis and might be of benefit in the dietic prevention of type 2 diabetes melitus (Bottin et al., 2011). Previous studies investigated the mechanisms by which mycoprotein reduces the rise in postprandial blood glucose and suggested that this might be associated with mycoprotein's high fibre content. They explained that fibre delays the passage of food into the small intestine (Leclere et al., 1994)

Another study investigated the impact of mycoprotein ingestions in a dose response manner on acute postprandial hyperaminoacidemia and hyperinsulinemia and the conclusions stated that mycoprotein represents a bioavailable and insulinotropic non-animal derived dietary protein. During

the study, mycoprotein was assessed both in comparison with a more typical animal-derived protein (milk protein) and in a dose response manner in young healthy men. Serum insulin, essential, non-essential and branched chain amino acids (BCAA) were of equivalent 4 hours postprandial availability after both mycoprotein and milk protein ingestion. Mycoprotein however, resulted in slower and lower peak plasma postprandial amino acid and insulin concentrations likely explained by delayed digestion and absorption kinetics as a result of the high fibre content. Results of this study suggested that, based on the observed bioavailability, ingestion of 40g of mycoprotein would be sufficient to mount a robust muscle protein synthetic response, with the ingestion of 60 g mycoprotein likely to provide an optimal anabolic response (Dunlop et al., 2017).

Work by Bottin et al. in 2012 has found that all doses of mycoprotein paste – 44, 88, and 132 g – significantly reduced 24-hour insulin levels compared with chicken controls that were closely matched for energy and macronutrient content when consumed by overweight and obese volunteers aged 18 to 65 years with a body mass index of 25 to 32 kg/m^2 (Bottin et al., 2012). The same author carried out a similar study a few years later and demonstrated that mycoprotein improves glycaemic profile (Bottin et al., 2016).

Group C results: Blood Lipids

With regard to cholesterol profile 1 study identified between the period 2002 – 2019. In 2010 a pilot study was conducted in order to test whether mycoprotein can lower blood cholesterol levels. The study showed a significant reducing effect of the intervention on the total cholesterol levels among the participants with higher baseline blood cholesterol levels (Ruxton CS and McMillan B, 2010). The findings confirmed that mycoprotein may be a useful food ingredient for helping to manage blood cholesterol levels. However, the sample of subjects of this study was small and therefore further work in a larger population is warranted, particularly to determine the optimal mycoprotein intakes and likely mechanisms of action. Improvements in cholesterol profiles may be attributed to the fact that mycoprotein does not contain cholesterol.

Finnigan et al. (2019) indicates that the cholesterol lowering effects of mycoprotein appear to be due to its high fibre content, coupled with its unique composition. In the same paper the authors noted that chitin and β-glucans create a fibrous, 88% insoluble matrix that may be a factor in delaying BCAA or glucose absorption, and impairing cholesterol or bile absorption. Their explanation from a series of previous studies is that bacterial metabolism of fibre in the gut may result in a greater production of short chain fatty acids that may affect cholesterol synthesis or lipolysis (Finnigan et al., 2019).

Group D results: Diet and Nutrition

The impact of mycoprotein on appetite regulation and hunger is also a topic that has been examined. In a study by Williamson et al., 42 overweight female participants consumed mycoprotein, chicken, or tofu followed by an ad-libitum lunch 20 minutes later and an ad-libitum dinner 4 hours after lunch (Williamson et al., 2006). Energy intake at lunch was significantly reduced following the consumption of mycoprotein compared with chicken. No differences in appetite visual analogue scales or in energy intake at the ad-libitum dinner were found. In a recent study, energy intake and appetite regulation in healthy overweight and obese volunteers was examined. The

results showed that consumption of 132 g of mycoprotein reduces energy intake by 10 % at an ad libitum meal compared with a macronutrient matched meal containing chicken (Bottin et al., 2016). The study indicated that if mycoprotein was consumed regularly and its effect maintained over the long term, this 10 % reduction in energy intake may represent a significant weight loss.

In general, the findings of the reviewed studies suggest that when mycoprotein is consumed as part of a healthy diet it has the potential of satiety effects and reduction of energy intake at subsequent meals. This is largely attributed to its high protein and fibre and low-fat profile. This in turn suggests that mycoprotein could potentially play a role in helping to support a healthy lipid profile and subsequent heart health. Ongoing randomized controlled trials using mycoprotein in healthcare settings would be worthy of continued investigation (Derbyshire and Ayoob, 2018).

Section 4: References

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APPENDIX B

Product description and intended use, Ref. FS02-D-001

Product Name: ABUNDA® Mycoprotein

1. Description

Mycoprotein is a food ingredient derived from a filamentous micro-organism, *Fusarium venenatum*, IMI145425. It is produced by an aerobic fermentation process, using a food grade carbohydrate substrate. The organism is unchanged from its natural state and has not been subject to any form of genetic manipulation.

ABUNDA mycoprotein is manufactured at a Pilot Plant in Europe under the project name Fulica. Individual mycoprotein batch runs have an identification code based on the pilot plant's fermenter utilised to run the product.

2. Raw materials and ingredients

- *Fusarium venenatum*
- Refined glucose or glucose syrups
- Deionised water

AND:

Chemical Formula	Substance Name	Legislation	Approved Food Additive (Y/N)
H_3PO_3	Phosphoric Acid	FDA Substances Added to Food	Y
$Ca(C_2H_3O2)_2$	Calcium Acetate	FDA Substances Added to Food	Y
$MgSO_4$ 7 H_2O	Magnesium sulfate heptahydrate	EC 1925/2006	Y
$CaCl_2$ 2 H_2O	Calcium Chloride dihydrate	EC 1129/2011	Y
K_2SO_4	Potassium sulfate	EC 1129/2011	Y
$ZnSO_4$ 7 H_2O	Zinc (II) sulfate heptahydrate	EC 1925/2006	Y
$MnSO_4$ H_2O	Manganese (II) sulfate monohydrate	EC 1925/2006	Y
$CuSO_4$ 5 H_2O	Copper (II) sulfate pentahydrate	EC 1925/2006	Y
$FeSO_4$ 7 H_2O	Iron (II) sulfate heptahydrate	EC 1925/2006	Y
$C_{10}H_{16}N_2O_3S$	Biotin	FDA Substances Added to Food	Y
$C_5H_{14}ClNO$	Choline Chloride	JECFA Approved	Y
NH_4OH	Ammonium hydroxide (25%)	FDA Substances Added to Food	Y
$FeCl_3$ 6 H_2O	Iron (III) chloride hexahydrate	EU 2015/1739 [(a)]	Y
Citric acid H2	Citric acid monohydrate	EC 1129/2011	Y
ZnCl2	Zinc chloride	EC 1925/2006	Y
MnCl2 4 H2O	Manganese (II) chloride tetrahydrate	EC 1925/2006	Y
CuCl2 2 H2O	Copper (II) chloride dihydrate	EC 1925/2006	Y
CoCl2 6 H2O	Cobalt (II) chloride hexahydrate	EFSA Opinion 2009 [(b)]	Y
Na2MoO4 2 H2O	Disodium molybdate dihydrate	EC 1925/2006	Y
KH2PO4	Potassium dihydrogen phosphate	FAO/WHO Food Additive Evaluations (JECFA)	Y
NH4Cl	Ammonium chloride	41st CAC 2018	Y

Notes:

[(a)] EFSA assessment of the safety of cobalt (II) chloride hexahydrate added for nutritional purposes as a source of cobalt in food supplements and the bioavailability of cobalt from this source.

[(b)] EFSA Scientific Opinion on the safety of the complexation product of sodium tartrate and iron (III) chloride as a food additive

3. Origin of the ingredients

MSDS documents available upon request

4. Chemical parameters (dry weight basis)

RNA:	< 2%
Protein:	not less than 42%
Ash:	< 5 %
Fat:	12 – 14 g

Heavy metals (dry weight basis):

Lead	- <0.1 mg/kg
Arsenic	- <0.1 mg/kg
Mercury	- <0.1 mg/kg
Cadmium	- <0.1 mg/kg

Mycotoxins: not detectable
Pesticides: meets the MRLs as these are set by relevant EC regulations.

5. Microbiological parameters

Pathogens:	Not detected
Total aerobic count:	≤ 100 cfu/g
Enterobacteriaceae:	< 10 cfu/g
Yeasts and Moulds:	≤ 100 cfu/g
Sulphite Red Clostridia:	< 10 cfu/g
Viable Fusarium:	Not detectable in 1g

6. Sensory parameters

Appearance:	Pale colour, dough like paste
Aroma:	Odourless
Texture:	Smooth dough like paste
Flavour:	Neutral taste

7. Typical Nutritional composition

Analyte (wet basis)	**Average (%)**
Moisture	75.00
Protein	13.00
Carbohydrates	4.7
Total Fat	1.7
Total Fiber	6.8
Energy	388
Calories	92
Sodium	< 0.1

8. Food safety requirements

Heat treated at a minimum 73°C for a minimum of 15 minutes.

9. Allergens contained

Tick the allergens contained in Regulation EU No. 1169/2011:

☐ 1. Cereals containing gluten, namely: wheat, rye, barley, oats, spelt, kamut or their hybridised strains, and products thereof
☐ 2. Crustaceans and products thereof
☐ 3. Eggs and products thereof
☐ 4. Fish and products thereof
☐ 5. Peanuts and products thereof

☐ 6. Soybeans and products thereof
☐ 7. Milk and products thereof (including lactose)
☐ 8. Nuts, namely: almonds, hazelnuts, walnuts, cashews, pecan nuts, Brazil nuts, pistachio nuts, macadamia or Queensland nuts, and products thereof
☐ 9. Celery and products thereof
☐ 10. Mustard and products thereof
☐ 11. Sesame seeds and products thereof
☐ 12. Sulphur dioxide and sulphites at concentrations of more than 10 mg/kg or 10 mg/litre in terms of the total SO2
☐ 13. Lupin and products thereof
☐ 14. Molluscs and products thereof

10. Legal requirements

The products correspond to the relevant UK and EU-jointly, food legislation, U.S. Federal Food Law, Australia New Zealand Food Standards Code.

11. Treatment and processing

Separation, filtration, where applicable followed by sterilization, fermentation, heat treatment, separation.

12. Packaging and consumption unit

TBC

13. Storage and distribution conditions

Frozen storage at - 20 °C (acceptable range between - 18 to -21°C).

14. Country of distribution

TBC

15. Minimum durability

Shelf life when frozen at least 12 months
Shelf life when chilled at least 72 hours when stored at 0-4 °C.

16. Risk assessment and main hazards

Development activities commenced in 2018 using refined glucose or glucose syrups and the chemical and nutritional composition of 3F BIO's mycoprotein is targeted to be identical to the specification detailed in the GRAS notice submitted to the US FDA (GRN No.91) in 2001. Since then, there have been 7 successful pilot production runs following lab scale trials and the results from ABUNDA® mycoprotein analysis (microbiological, nutritional, chemical and physical) confirm product's consistency and is also comparable to the existing mycoprotein specification. Evaluation of safety data on existing mycoprotein products supports the conclusion that the proposed uses would not be expected to produce any acute or chronic adverse effects. Market information on typical levels and frequency of consumption of existing mycoprotein products, leads to the conclusion that the use of mycoprotein will not be expected to produce any acute or chronic adverse effects in individuals consuming these food products under the intended conditions of use.

Although mycoprotein is obtained from a fungus, when mycoprotein is grown and harvested correctly, mycotoxins are not produced during the production process. All analytical data gathered from the pilot runs, meet the requirements as those are laid down in Regulation (EC) No 1881/2006. Potential pathogenic bacteria naturally present in the environment - i.e. *Salmonella Species, Enterobacter Species, Campylobacter Species, Listeria Monocytogenes and Staphylococcus Species*, will be destroyed by the heat treatment process, thereby negating any potential health risk. As regards to *Staphylococcus aureus*, the bacterium will not form a toxin at temperatures <15°C. Mycoprotein is kept at a target temperature of < 4°C when chilled or below -18°C when frozen. Significant levels of bacteria/toxin are needed to be present to be considered harmful. All mycoprotein batches produced during the pilot runs are going through metal detection at the end of each pilot run.

Relevant Legislation:

- The Food Hygiene, Scotland, Regulations 2005
- Regulation (EC) No 852/2004 on the Hygiene of foodstuffs Article 5
- Regulation (EC) No 1881/2006 on setting maximum levels for certain contaminants in foodstuffs
- Regulation (EC) No 1169/2011 on the provision of food information to consumers
- Regulation (EC) No 2073/2005 on microbiological criteria for foodstuffs
- US GRAS notification for mycoprotein (November 2001)
- EFSA Journal 2011;9(9):2353 - Scientific Opinion on safety and efficacy of choline chloride as a feed additive for all animal species
- Federation of American Societies for Experimental Biology, 1975
- FSANZ, 2018 - Compendium of Microbiological Criteria for Food

17. Provided intended use (and possible misuse)

Mycoprotein is suitable for incorporation into a wide variety of foods. Because of its textural and nutritional characteristics mycoprotein may be processed into products used as an alternative to meat in a variety of meals. For example, it may be used in beef burgers as meat replacement, as a protein ingredient in noodles, or as the main ingredient for chicken style fillet. Mycoprotein is not intended to be consumed raw.

Mycoprotein provides good nutrition, convenience, and an appropriate texture, due to its inherent hyphal structure. This characteristic enables a wide range of properties to be achieved when the product is used as an ingredient, including meat-like properties, fat-like properties, or cereal-like properties.

Should be kept frozen at - 20 °C (acceptable range between - 18 to -21°C). The recommended process for defrosting mycoprotein is to hold it in a chilled (0-4 °C) environment for at least 24 hours. Once product is fully thawed it has a 72 hours shelf life in refrigerated storage. Product should not be re - frozen after thawing.

18. Target groups and their specialities

Consumer group	**Suitability**		**Comment**
	YES	**NO**	
Babies < 12 months		x	
Infants 1 to 3 years		x	
Children/ youth 4 to 18 years	x		
Adults 19 to 65 years	x		
Seniors > 65 years	x		
Pregnant women	x		
Breast-feeding mothers	x		
Sick or immuncompromised people	x		
Allergy sufferers	x		

Appendix C

Example laboratory reports (including microbiology, toxic elements, amino acids, vitamins, basic nutritional).

SYNLAB

UKAS TESTING 4412

CERTIFICATE OF ANALYSIS

FAO:	Yogeshwar Chandelia	Order Number:	PO-0275
Company:	3FBIO Ltd	Date Received:	11/12/2019
Address:	Suite 4.1 135 Buchanan Street Glasgow G1 2JA	Report Date:	27/03/2020
		Start Date:	12/12/2019
		Report Number:	19-35783/2
		Testing Suite	3FBIO001

Lab No:	1728961	Specification	3FBIO001
Product Code:			
Client Reference:	Day 1		
Sample Description:	Shelf Life Chilled - FULICA4F03_6H_BAG 1		
Use by	/ /		
Customer	3F BIO Ltd		
Additional Info.	1 dilution for ACC, Pseuds and Yeasts		

Test Ref	Analysis	Result	Units
MIC1004	Aerobic Colony Count 72h at 30ºC	< 10	cfu/g
MIC1005	Moulds	< 20	cfu/g
MIC1005	Yeasts	< 20	cfu/g
MIC1018	Enterobacteriaceae (presumptive)	< 10	cfu/g
MIC1021	Coagulase Pos Staphylococci (Presumptive	< 20	cfu/g
MIC1022	E. coli (presumptive)	< 10	cfu/g
MIC1025	Pseudomonas spp. (presumptive)	< 20	cfu/g
MIC1027	Clostridium perfringens (presumpt)	< 10	cfu/g
MIC1023	Salmonella spp. (detection)	Not Detected	in 25g
MIC1056	Sulphite Reducing Clostridia	< 10	cfu/g

Signed for and on behalf of SYNLAB

Phil Marsden, Data Systems Manager

All tests reported above are ISO 17025 accredited unless marked with a *.
Tests marked with a @ have been subcontracted to a ISO 17025 Accredited laboratory

The Test results published in this report relate only to the stated sample description as received by the laboratory

Any limits applied to results are as agreed with the customer

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SYNLAB

UKAS TESTING
4412

CERTIFICATE OF ANALYSIS

FAO:	Yogeshwar Chandelia	Order Number:	PO-0275
Company:	3FBIO Ltd	Date Received:	11/12/2019
Address:	2nd Floor Spaces 100 West George Street Glasgow Lanarkshire	Report Date:	18/12/2019

Lab No:	**90085574**	Report Number:	19-09025
Client Reference:	**Fulica4F03**		
Sample Description:	**RNA analysis**		
Product Code:	**BAG 8_RETAINED_480G**		

Test Ref	Analysis	Result	Units
CHEM013	Moisture	75.8	g/100g
CHEM013	Dry Matter	24.2	g/100g
CHEM020	RNA in Dry Matter*	1.0	g/100g
SUBCON	RNA*	0.24	g/100g

Signed for and on behalf of SYNLAB

Sam Whalan, Chemistry Lab Manager

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Samples marked with a ‡ are subcontracted to a UKAS accredited laboratory

The results reported relate only to the items tested.

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SYNLAB

UKAS TESTING 4412

CERTIFICATE OF ANALYSIS

FAO: Yogeshwar Chandelia
Company: 3FBIO Ltd
Address: Suite 4.1
135 Buchanan Street
Glasgow
G1 2JA

Order Number: PO-0275
Date Received: 11/12/2019
Report Date: 20/01/2020

Lab No: **90085575**
Client Reference: **Fulica4F03**
Sample Description: **Full analysis**
Product Code: **BAG 20_RETAINED**

Report Number: 19-09025/2

Test Ref	Analysis	Result	Units
SUBCON	Aspartic Acid/asparagine‡	1.18	g/100g
SUBCON	Ochratoxin A (OTA)‡	< 0.10	µg/kg
SUBCON	Potassium‡	1000	mg/kg
SUBCON	Nicotinic acid‡	< 0.1	mg/100g
SUBCON	Nicotinamide‡	0.2	mg/100g
SUBCON	Serine (Total)‡	0.55	g/100g
SUBCON	Aflatoxin B1‡	< 0.1	µg/kg
SUBCON	(Total Vitamin B3)‡	0.30	mg/100g
SUBCON	Glutamic Acid (Total)‡	1.38	g/100g
SUBCON	Aflatoxin B2‡	< 0.1	µg/kg
SUBCON	Glycine (Total)‡	0.55	g/100g
SUBCON	Aflatoxin G1‡	< 0.1	µg/kg
SUBCON	Histidine (Total)‡	0.30	g/100g
SUBCON	Aflatoxin G2‡	< 0.1	µg/kg
SUBCON	Arginine (Total)‡	0.77	g/100g
SUBCON	Aflatoxin Total‡	Not Detected	µg/kg
SUBCON	Theonine (Total)‡	0.62	g/100g
SUBCON	Aflatoxin M1‡	< 0.05	µg/kg
SUBCON	Alanine (Total)‡	0.76	g/100g
SUBCON	Patulin‡	< 10.0	µg/kg

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Page: 1 of 3

SUBCON	Zearalenone (F2 / ZON or ZEA)‡	< 3.0	µg/kg
SUBCON	Proline (Total)‡	0.51	g/100g
SUBCON	Cystine (Total)‡	0.09	g/100g
CHEM020	Energy	324	kJ/100g
SUBCON	Fumonisin B1‡	< 10	µg/kg
SUBCON	Tyrosine (Total)‡	< 0.30	g/100g
SUBCON	Fumonisin B2‡	< 10	µg/kg
SUBCON	Valine (Total)‡	0.69	g/100g
SUBCON	Fumonisin B3‡	< 10	µg/kg
SUBCON	3 Acetyldeoxynivalenol (3AcDON)‡	< 10	µg/kg
SUBCON	Methionine (Total)‡	0.21	g/100g
SUBCON	15 Acetyldeoxynivalenol (15AcDON)‡	< 10	µg/kg
SUBCON	Lysine (Total)‡	0.91	g/100g
SUBCON	Deoxynivalenol (DON)‡	< 10	µg/kg
SUBCON	Iso-Leucine (Total)‡	0.56	g/100g
SUBCON	Diacetoxyscirpenol (DAS)‡	< 10	µg/kg
SUBCON	Leucine (Total)‡	0.82	g/100g
SUBCON	Fusarenone X (Fus X)‡	< 10	µg/kg
SUBCON	Phenylalanine (Total)‡	0.46	g/100g
SUBCON	HT2 Toxin (HT2)‡	< 10.0	µg/kg
SUBCON	Tryptophan (Total)‡	0.16	g/100g
SUBCON	T2 Toxin (T2)‡	< 10.0	µg/kg
SUBCON	Neosolaniol (NEO)‡	< 10	µg/kg
CHEM020	Calories	76	kcal/100g
SUBCON	Nivalenol (NIV)‡	< 10	µg/kg
CHEM013	Moisture	79.6	g/100g
CHEM024	Nitrogen	1.82	g/100g
CHEM024	Protein (Nitrogen x 6.25)	11.4	g/100g
CHEM022	Total Fat	0.9	g/100g
CHEM016	Saturated Fat	0.4	g/100g
CHEM016	Mono-unsaturated Fat	0.3	g/100g
CHEM016	Poly-unsaturated Fat	0.2	g/100g
CHEM016	Trans-unsaturated Fat	< 0.1	g/100g
CHEM020	Total Carbohydrate	5.7	g/100g
CHEM012	Dietary Fibre (AOAC)	7.2	g/100g
CHEM014	Ash	0.6	g/100g
CHEM009	Sodium	< 0.01	g/100g
CHEM009	Sodium‡	12.0	mg/kg
CHEM020	Salt (Sodium x 2.50)	0.01	g/100g
SUBCON	Zinc‡	110	mg/kg
SUBCON	Lead‡	0.0280	mg/kg
SUBCON	Copper‡	5.90	mg/kg

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SUBCON	Arsenic‡	< 0.005	mg/kg
SUBCON	Cadmium‡	< 0.0004	mg/kg
SUBCON	Mercury‡	< 0.0020	mg/kg
SUBCON	Folate(Vitamin B9)‡	144.0	µg/100g
SUBCON	Vitamin D2‡	< 0.50	µg/100g
SUBCON	Iron‡	2.00	mg/kg
SUBCON	Calcium‡	160.0	mg/kg
SUBCON	Manganese‡	18.0	mg/kg
SUBCON	Magnesium‡	230	mg/kg
SUBCON	Phosphorus‡	1300	mg/kg
SUBCON	Biotin‡	< 0.5	µg/100g
SUBCON	Pantothenic Acid‡*	0.21	mg/100g
SUBCON	Vitamin B2 (Riboflavin)‡	0.10	mg/100g
SUBCON	Vitamin B1 (as Thiamine Hydrochloride)‡	< 0.0100	mg/100g

Signed for and on behalf of SYNLAB

Phil Marsden, Data Systems Manager

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Form Approved: OMB No. 0910-0342; Expiration Date: 07/31/2022
(See last page for OMB Statement)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

GENERALLY RECOGNIZED AS SAFE *(GRAS)* NOTICE (Subpart E of Part 170)

FDA USE ONLY

GRN NUMBER	DATE OF RECEIPT
000945	Jun 2, 2020
ESTIMATED DAILY INTAKE	INTENDED USE FOR INTERNET
NAME FOR INTERNET	
KEYWORDS	

Transmit completed form and attachments electronically via the Electronic Submission Gateway *(see Instructions)*; OR Transmit completed form and attachments in paper format or on physical media to: Office of Food Additive Safety *(HFS-200)*, Center for Food Safety and Applied Nutrition, Food and Drug Administration,5001 Campus Drive, College Park, MD 20740-3835.

1. Type of Submission *(Check one)*

☒ New ☐ Amendment to GRN No. _____ ☐ Supplement to GRN No. _____

2. ☒ All electronic files included in this submission have been checked and found to be virus free. *(Check box to verify)*

3 Most recent presubmission meeting *(if any)* with FDA on the subject substance *(yyyy/mm/dd):* 2020-05-28

4 For Amendments or Supplements: Is your amendment or supplement submitted in response to a communication from FDA? *(Check one)* ☐ Yes ☐ No If yes, enter the date of communication *(yyyy/mm/dd):* _____

Name of Contact Person	Position or Title
Sofia Mavromati	Mrs
Organization *(if applicable)*	
3F BIO Ltd	
Mailing Address *(number and street)*	
135 Buchanan Street Suite 4.1	

City	State or Province	Zip Code/Postal Code	Country
Glasgow	Lanarkshire	G1 2JA	United Kingdom

Telephone Number	Fax Number	E-Mail Address
07767412809		sofia.mavromati@3fbio.com

Name of Contact Person	Position or Title
Organization *(if applicable)*	
Mailing Address *(number and street)*	

City	State or Province	Zip Code/Postal Code	Country

Telephone Number	Fax Number	E-Mail Address

SECTION C – GENERAL ADMINISTRATIVE INFORMATION

1. Name of notified substance, using an appropriately descriptive term

Common name is mycoprotein derived from Fusarium venenatum. The trade name is ABUNDA mycoprotein.

2. Submission Format: *(Check appropriate box(es))*

☒ Electronic Submission Gateway

☐ Electronic files on physical media

☐ Paper

If applicable give number and type of physical media

_____

3. For paper submissions only:

Number of volumes _____

Total number of pages _____

4. Does this submission incorporate any information in CFSAN's files? *(Check one)*

☒ Yes *(Proceed to Item 5)* ☐ No *(Proceed to Item 6)*

5. The submission incorporates information from a previous submission to FDA as indicated below *(Check all that apply)*

☒ a) GRAS Notice No. GRN 000091

☐ b) GRAS Affirmation Petition No. GRP _____

☐ c) Food Additive Petition No. FAP _____

☐ d) Food Master File No. FMF _____

☐ e) Other or Additional *(describe or enter information as above)* _____

6. Statutory basis for conclusions of GRAS status *(Check one)*

☒ Scientific procedures *(21 CFR 170.30(a) and (b))* ☐ Experience based on common use in food *(21 CFR 170.30(a) and (c))*

7. Does the submission (including information that you are incorporating) contain information that you view as trade secret or as confidential commercial or financial information? (see 21 CFR 170.225(c)(8))

☐ Yes *(Proceed to Item 8*

☒ No *(Proceed to Section D)*

8. Have you designated information in your submission that you view as trade secret or as confidential commercial or financial information *(Check all that apply)*

☐ Yes, information is designated at the place where it occurs in the submission

☐ No

9. Have you attached a redacted copy of some or all of the submission? *(Check one)*

☐ Yes, a redacted copy of the complete submission

☐ Yes, a redacted copy of part(s) of the submission

☐ No

SECTION D – INTENDED USE

1. Describe the intended conditions of use of the notified substance, including the foods in which the substance will be used, the levels of use in such foods, and the purposes for which the substance will be used, including, when appropriate, a description of a subpopulation expected to consume the notified substance.

3F BIO is intending to sell their substance as a food ingredient on a B2B basis for it to be used in a variety of meals - excluding meat, poultry and infant formula. Levels of use in these meals is expected to be between 10% and 90%.

2. Does the intended use of the notified substance include any use in product(s) subject to regulation by the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☒ No

3. If your submission contains trade secrets, do you authorize FDA to provide this information to the Food Safety and Inspection Service of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☐ No , you ask us to exclude trade secrets from the information FDA will send to FSIS.

SECTION E – PARTS 2 -7 OF YOUR GRAS NOTICE

(check list to help ensure your submission is complete – PART 1 is addressed in other sections of this form)

☒ PART 2 of a GRAS notice: Identity, method of manufacture, specifications, and physical or technical effect (170.230).

☒ PART 3 of a GRAS notice: Dietary exposure (170.235).

☒ PART 4 of a GRAS notice: Self-limiting levels of use (170.240).

☒ PART 5 of a GRAS notice: Experience based on common use in foods before 1958 (170.245).

☒ PART 6 of a GRAS notice: Narrative (170.250).

☒ PART 7 of a GRAS notice: List of supporting data and information in your GRAS notice (170.255)

Other Information

Did you include any other information that you want FDA to consider in evaluating your GRAS notice?

☐ Yes ☒ No

Did you include this other information in the list of attachments?

☐ Yes ☐ No

1. The undersigned is informing FDA that Sofia Mavromati
(name of notifier)

has concluded that the intended use*(s)* of Common name is mycoprotein derived from Fusarium venenatum. The trade name is ABUNDA
(name of notified substance)

described on this form, as discussed in the attached notice, is (are) not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on your conclusion that the substance is generally recognized as safe recognized as safe under the conditions of its intended use in accordance with § 170.30.

2. Sofia Mavromati agrees to make the data and information that are the basis for the conclusion of GRAS status available to FDA if FDA asks to see them; agrees to allow FDA to review and copy these data and information during customary business hours at the following location if FDA asks to do so; agrees to send these data and information to FDA if FDA asks to do so.
(name of notifier)

135 Buchanan Street, 4.1, Glasgow, G1 2JA, United Kingdom
(address of notifier or other location)

The notifying party certifies that this GRAS notice is a complete, representative, and balanced submission that includes unfavorable, as well as favorable information, pertinent to the evaluation of the safety and GRAS status of the use of the substance.The notifying party certifies that the information provided herein is accurate and complete to the best or his/her knowledge. Any knowing and willful misinterpretation is subject to criminal penalty pursuant to 18 U.S.C. 1001.

3. Signature of Responsible Official, Agent, or Attorney	Printed Name and Title	Date (mm/dd/yyyy)
sofia.mavromati@3fbio.com Digitally signed by sofia.mavromati@3fbio.com Date: 2020.06.02 16:41:10 +01'00'	Sofia Mavromati, Food Safety & Quality Manager	06/02/2020

SECTION G – LIST OF ATTACHMENTS

List your attached files or documents containing your submission, forms, amendments or supplements, and other pertinent information. Clearly identify the attachment with appropriate descriptive file names (or titles for paper documents), preferably as suggested in the guidance associated with this form. Number your attachments consecutively. When submitting paper documents, enter the inclusive page numbers of each portion of the document below.

Attachment Number	Attachment Name	Folder Location (select from menu) (Page Number(s) for paper Copy Only)
	Form3667.pdf	Administrative
	GRAS Notice-2020-06-02.pdf	GRAS Notice