



## **Opinion on the Safety of BioProtein® by the Scientific Panel on Animal Feed of the Norwegian Scientific Committee for Food Safety**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. The opinion has been assessed and approved by the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of VKM. All authors read and approved the final manuscript.*

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### **ABSTRACT**

BioProtein® (BP) is a trademark for single cell (bacteria) protein, based on conversion of methane, with the addition of ammonia and oxygen, to a protein source. BP is produced by Norferm AS in Norway, and has been authorized by the EU as a protein source in animal feeds since 1995, for fattening pigs (8%), calves (8%) and salmon (19-33%). Significant immune effects were revealed in a toxicity study performed in rats fed a nucleic acid reduced BP product (NABP) and thereafter, similar, but less severe effects were also found after feeding with untreated BP. Additional studies confirmed increased mesenteric lymph node weights in cats and foxes. Due to the undesirable effects and also due to applications for extended use, BP has been assessed by the Scientific

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Committee on Animal Nutrition (SCAN) and EU's Scientific Committee on Food (SCF) in 1995, by SCAN in 2001 and 2003 and by the European Food Safety Authority (EFSA) in 2005. The EU memberstates United Kingdom, France and Finland have also conducted assessments. The EU approval from 1995 remains unchanged.

The Norwegian Food Safety Authority requested the Norwegian Scientific Committee for Food Safety (VKM) to assess the risk of using BP as a protein source in feedingstuffs, both for the animal categories already authorized and for extended use to pet animals, chickens and pigs from weaning to slaughter. The Norwegian Scientific Committee for Food Safety was asked to consider all existing documentation. Based on all documentation enclosed with the request from the Norwegian Food Safety Authority and published scientific articles, an opinion on the safety of BP assessed by the VKM panel on Animal Feed was published on 20 March 2006 (05/608-final-rev1). The Producer made a complaint regarding this opinion and claimed that not all documents on BP had been evaluated. The Norwegian Food Safety Authority then requested VKM to revise its opinion on the risk of using BP as a protein source in feedingstuffs, based on 17 documents previously not available to VKM, in addition to the 20 documents included in the opinion published on 20 March 2006.

BP is composed of a protein with a somewhat different amino acid composition compared with fish meal, but BP and fish meal have more similarities in amino acid content than soybean meal. BP has relatively high level of nucleic acids, phospholipids, lipopolysaccharides and minerals.

Effect studies with BP have been conducted in rats/mice, pigs, chicken, cats, foxes, and salmon. Most of the concern regarding the side effects of BP in feed is related to the immune response. The main findings include changes in weight and morphology of mesenteric lymph nodes, followed by induction of specific antibodies. Histopathological examination after feeding with NABP also revealed changes in the intestines and several internal organs indicating systemic effects. The Producer claims that the immune response seen in BP-fed mice/rats is most likely a normal response to ingestion of large doses of a foreign antigen, and further, that oral tolerance towards this protein is induced over time. However, these interpretations are not adequately supported by the supplied documentation. A tendency towards adaptation might be indicated in some of the studies, other results argue against tolerance induction.

It is unclear whether the content of phospholipids, lipopolysaccharides, nucleic acids or the protein structure, or the combination of these compounds is responsible for the immunological changes observed. However, the particulate structure of BP has been shown to influence the observed immune response as the systemic immune response was avoided by ingestion of BP free of whole cells.

The studies conducted in target species have not included adequate examinations of the immune effects from ingestion of BP. Concerning terrestrial species, no histopathological effects were revealed in the pig, chicken, cat or fox studies. However, increased mesenteric lymph nodes were reported in cats and foxes fed BP. In the remaining studies the main focus has been on production parameters; weight gain, feed intake, feed efficiency, metabolism of nutrients, observation of clinical health, and product quality. When the contents of amino acids were balanced, the inclusion of low levels of BP (9%) tended to stimulate growth in pigs and the same tendency was found in chicken with 6% BP. Higher feed levels of BP tended to cause a reduction in growth.

In salmon, a dose dependent improvement of growth was reported in a short term experiment (8 weeks). However, in longer term experiments with salmon, depressed growth and increased liver weight were observed in freshwater at 19% BP with no-effect-level at 10%. In seawater studies, a tendency of reduced growth was found in salmon fed with 20% BP in the diet, and BP levels of 27% and higher levels resulted in significantly reduced body weight. Furthermore, levels of 27% BP and above in fish feed reduced specific immune responses, but increased lymphocyte response, and also tended to improve the survival after bacterial and viral infections. At 37% BP in the diet histopathological changes in the distal intestine, and reduced storage of glycogen and increased lipid deposition and liver weight were observed. No negative effects were seen in

salmon in seawater at a feed level of 13.5% BP. The results indicate negative effects in salmon at BP levels in fish feed considerably lower than those currently approved (19 and 33%, in feed for salmon in fresh and sea water, respectively).

To conclude, in terrestrial target species documented effects of BP include reduced weight gain and increased weight of mesenteric lymph nodes. In the more thoroughly studied species the rat, findings include histopathologic effects in mesenteric lymph nodes, changed humoral immune responses, increased weight of other lymphoid tissue (spleen), increased level of neutrophile granulocytes, and slight leakage of hepatic and renal tubuli enzymes. In terrestrial target species, 6% BP in the feed is considered to be the highest inclusion level not to cause such effects. The results from the rat studies show a similar no-effect-level. In salmon, reduced weight gain, liver storage effects, changed humoral and cellular immune responses and histopathological effects in the intestine are documented. A 10% level of BP in fish feed is the highest level tested without causing such effects. There are relatively few valid studies for the risk assessment of BP in target species, and the designs of the assessed studies are very variable. Thus, there are qualitative and quantitative uncertainties concerning the effects of BP in target species. The Panel on Animal Feed is of the opinion that an inclusion level of BP of 6% in the diets to terrestrial target animals and a 10% maximum inclusion level in salmon feed (both for fresh- and seawater stages) would reduce the risk of potentially adverse effects in the animals.

The risk associated with the human consumption of products from animals fed on BP is considered negligible. However, the production of single cell protein for feed production represents a relatively new scientific approach which implies precautionary handling.

**Keywords:** *BioProtein; Single Cell Protein; animal safety; food safety; health; immune effect; animal feed; VKM; assessment; Norwegian Scientific Committee for Food Safety.*

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#### **NOTE:**

This work was carried out in collaboration between all authors. The opinion has been assessed and approved by the Opinion of the Panel on Animal Feed of the Norwegian Scientific Committee for Food Safety (VKM). All authors read and approved the final manuscript.

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#### **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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