Letter to the Editor

Probiotic and prebiotic claims in Europe: seeking a clear roadmap

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In 2008, the European Food Safety Authority (EFSA) began reviewing the proposed health benefit claims on all foods.

To date, none of the 164 claims of the benefits of probiotic or prebiotic products submitted to EFSA and reviewed by the Panel on Dietetic Products, Nutrition, and Allergies (NDA) have been accepted (see Table 1). Those who are not aware of either the research supporting specific probiotics and prebiotics or the NDA review process may come to the fallacious conclusion that probiotics or prebiotics have not been shown to have health benefits. Without doubt, fraudulent or exaggerated claims are being made for some products. However, the scientists and clinical investigators belonging to the Board of Directors of the International Scientific Association for Probiotics and Prebiotics (ISAPP) are concerned that claims supported by solid scientific evidence are also being rejected. They are further concerned that there is a lack of clarity regarding the criteria – from study design through wording of the claim – for a dossier suitable for a positive regulatory opinion. One unintended consequence of the current review process may well be that the responsible companies studying the physiological effects of their probiotic or prebiotic products will decide that continued investment into this line of research is not cost-effective if, in the end, evidence supporting product benefits deemed valid by the scientific community cannot be communicated to the consumer.

Certainly, evaluation of evidence to support claims is not a simple process. The NDA scientists must implement challenging legislation and assess a flood of dossiers providing evidence, which in the nature of all research could always be improved. But the process is difficult for industry scientists, too, who must prepare a dossier in support of a claim with only general guidance from the NDA. A successful dossier requires not only compelling studies on efficacy, but also specification of a physiological effect that will be considered by the NDA as beneficial and a claim that is worded to accurately reflect the science but also be in compliance with regulations. Some recent documents have been drafted by the NDA to provide guidance on their interpretation of what constitutes beneficial effects and acceptable outcome measures (http://www.efsa.europa.eu/en/consultationsclosed/call/nda100928.pdf), but many questions remain unanswered. This opinion is reflected in a letter (http://www.gut-health.eu) by the European scientists expressing dissatisfaction with the process. As of 23 February 2011, 148 scientists have signed this letter.

One overriding concern with the review process is the standard of evidence required by the NDA. The legislation states that ‘Health claims should only be authorised for use in the Community after a scientific assessment of the highest possible standard’. However, this seems to be interpreted by the NDA to mean that the evidence (as opposed to the assessment) must meet the highest possible standard. A more realistic standard is expressed in article 6 of the EC Regulation 1924/2006, which states that health claims shall be based on and substantiated by ‘generally accepted scientific evidence’. Thus, regulators have indicated a definite roadmap: generally accepted scientific evidence is not the same as the notion that evidence must be based on a restrictive number of criteria established by the scientific community.

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lacking statistical significance (although such findings clearly
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results), is a more reasonable approach.
Many of these difficulties could be resolved to the ultimate
benefit of the European Union Community. A mechanism for
pre-application meetings should be instituted. This would
enable companies to gain NDA feedback on a research
approach before launching expensive and time-consuming
studies. Increased use of scientific experts to augment the
NDA panel could provide the expertise and perspective
needed for a greater diversity of viewpoints and better balance
to the evaluation process. And finally, the NDA should adjust
its approach on what it requires as the standard of evidence.
A requirement of evidence of the ‘highest possible standard’
aged over 50.(2) Yet the NDA deemed the evidence in this study
as not of sufficiently high quality to support communication of
the protective effect of the product against antibiotic-associated
diarrhoea and C. difficile toxin production. Treatment costs per
patient for C. difficile-associated diarrhoea are on average $3669
in the USA(4) and £4000 in the UK(5). The availability of a safe,
dietary approach to reduce the morbidity of such conditions
should be hailed, not suppressed.
Another concern is that the panel appears to conclude that
unless all studies support the relationship being claimed, the
totality of evidence is not compelling. However, we should
not conclude that a study with a primary end point that
does not reach statistical significance represents contradictory
evidence. Studies on foods are often characterised by small
magnitudes of effects and insufficient power to detect them
at an acceptable level of statistical significance, placebos that
may not be fully inert, high variability in study group subjects
due to confounding factors such as background diet and indi-
vidual microbiota, and a study group that is healthy, which
makes it difficult to measure physiologically relevant changes.
On the other hand, results from study populations that are
more susceptible are considered irrelevant by the panel for
the general population. Considering these factors, an under-
powered study that does not yield statistically significant posi-
tive results should not be used to negate the outcomes of
other positive studies. Assessing the preponderance of evi-
dence, including magnitudes of effect observed in studies
lacking statistical significance (although such findings clearly
may be unrealistic for a functional food that is proposed to
maintain health or reduce risk of disease. In keeping with
the legislation, EFSA should strive for an assessment process
of the ‘highest possible standard’. This would be a process
that correctly evaluated the degree of support for a claim
that properly interpreted studies, that evaluated the strengths
and weaknesses of studies to determine their true worth,
and that, overall, had mechanisms in place to assure that the
spirit of the legislation is upheld. (It would also include
proper distinctions between ‘probiotic’ and ‘prebiotic’, which
were confused in the NDA opinion on lactulose(60).) Such
mechanisms would include the pre-application meetings and
use of ad hoc experts.
In the end, such changes would prevent the use of unsub-
stantiated claims on food products in the European market-
place while allowing communication of science that is
suitably compelling. Finally, such changes would provide
industry with a clear roadmap to understanding what is
required to gain approval for a health claim on food, so that
further investment in research is encouraged.
ISAPP is a non-profit scientific society that brings together
independent academic and industrial scientists involved in
research on fundamental and applied aspects of probiotics
and prebiotics, to forward its mission of fostering high-quality
research and scientific communication in the fields of probio-
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3. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2010) Scientific opinion on the substantiation of a health claim related to fermented milk containing Lactobacillus casei DN-114 001 plus yoghurt symbiosis (Actimel®), and reduction of Clostridium difficile toxins in the gut of patients receiving antibiotics and reduced risk of acute diarrhoea in patients receiving antibiotics pursuant to Article 14 of Regulation (EC) no. 1924/2006. EFSA J 8, 1903. www.efsa.europa.eu/efsajournal.htm


6. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2010) Scientific opinion on the substantiation of health claims related to lactulose and decreasing potentially pathogenic gastro-intestinal microorganisms (ID 806) and reduction in intestinal transit time (ID 807) pursuant to Article 13(1) of Regulation (EC) no. 1924/2006. EFSA J 8, 1806.