GENERAL MILLS

September 14, 2017

BY ELECTRONIC DELIVERY

RE: Response to Food Standards Australia New Zealand (FSANZ) Consultation Paper – W1109 – Consultation about beta-glucan and blood cholesterol health claims

Dear Sir or Madam:

General Mills (GMI) is a major packaged-food manufacturer engaged for over 150 years in the development and production of food products including ready-to-eat-cereals, yogurts, vegetables, soups, snacks, flour, cake and other dessert mixes, refrigerated dough and numerous other products. Our company's purpose is simple but powerful: we serve the world by making food people love. Embedded in this purpose is a deep respect and sense of service to our consumers and a commitment to understanding their needs and expectations. To help meet our consumers' health and nutrition needs, we have been committed to accurate and responsible communication of the benefits of foods and food groups as part of the overall diet.

General Mills has been and continues to be a leader in whole grain research, including expanding our understanding of whole grain intake on public health and agricultural improvements of grains. We appreciate the opportunity to review FSANZ's consult paper and comment on the scientific review regarding oats, barley, and beta-glucan.

Summary:

1) Regarding the assessment of the relationship between oats and blood cholesterol, General Mills agrees that the scientific evidence is sufficient to substantiate high level and general level health claim (HLHC, GLHC), but disagrees with FSANZ regarding their conclusion of the evidence for barley.

2) FSANZ inappropriately downgraded the evidence for barley and blood cholesterol to "moderate" citing too few subject numbers in the clinical trials. Results of all trials included were found to consistently favor barley versus control and the results were significant. Increasing subject number would only serve to increase the level of significance or narrow the confidence interval for the current results. FSANZ provided no data to justify downgrading the evidence.

3) FSANZ's systematic review of the evidence of a relationship between oats, barley and their derived beta-glucan on blood cholesterol concentration identified no research supporting *pure* beta-glucan for effect on cholesterol outside the matrix of oats or barley. General Mills points out that it is not reasonable to evaluate *pure* beta-glucan in a dietary trial and highlights that this new, unexpected standard for scientific substantiation unreasonably shifts expectations from food to a pharmaceutical model.

4) Beta-glucan is an important component of regulatory compliance for oat and barley HLHC. Research has shown that a minimum amount of beta-glucan from oat and barley was necessary to demonstrating positive effects on blood cholesterol, hence the recommendation for 3 grams per day. Any proposed changes to the oats and barley HLHC language should not discount the role beta-glucan plays to ensure delivery of meaningful amounts in a food serving. For example, health claims in Australia, the EU and the USA require beta-glucan at between 0.75 and 1 gram per serving as a result of the dietary research on health outcomes.

5) Unintended consequences that compromise public health may result if FSANZ was to not maintain support for oats and barley beta-glucan. Australian dietary guidance promotes the consumption of barley and oats – which research concludes is connected to the beta-glucan content. Withdrawing support for consumer recognized claims on beta-glucan and barley in conflict with the dietary guidance would conceivably erode consumer trust in nutrition science and may even result in reduced intake of whole grains.

Australia's high level health claim (HLHC) regarding the association between oat beta-glucan and barley beta-glucan is consistent with independent reviews of the evidence by other respected global authorities, including the United States Food and Drug Administration, the European Food Safety Authority, and Health Canada. The examination of the evidence by these groups also aligned with expert opinion that based their position on both strong epidemiological data and the plausible mechanism of oat and barley beta-glucans to reduce blood cholesterol concentrations as observed in multiple clinical trials. In light of the consensus positions from authoritative sources and experts conducting research in this field, FSANZ's recent scientific review and conclusions drawn from the data is challenging to comprehend.

General Mills provides the following comments in response to FSANZ's consult paper and the scientific review.

Oats

FSANZ's scientific review of the effect of oats on reducing blood cholesterol concentrations confirms earlier research and is consistent with positions by global regulatory authorities. General Mills agrees with the findings and conclusions regarding whole grain oats and oat bran with beta-glucan and is supportive of a high level and general level health claim for whole grain

oats and oat bran. It should also be noted that the totality of the evidence has indicated a minimum of approximately 3 grams of beta-glucan from oats was associated with the effect. As a result, it is logical to include a minimum threshold for beta-glucan in the whole grain oat health claims to ensure a meaningful amount is present in the food serving (e.g., between 0.75 and 1 gram).

Barley

General Mills asks FSANZ to recognize the data in their scientific review that support barley's ability to significantly reduce total and LDL-cholesterol in the blood and maintain barley in the high level and general level health claims, as previously approved.

General Mills wishes to highlight the inconsistency between FSANZ conclusion and the results of FSANZ's science review regarding barley and blood cholesterol. The systematic review states "*The relationship between barley and blood total and LDL cholesterol concentrations was shown to be consistent, with plausible mechanisms to explain the observed effect*". However, the conclusion indicates the confidence in the evidence was downgraded to "Moderate" degree of certainty because of low test subject numbers. Typically, studies are unable to reach significance without a sufficiently large subject population. In these studies, significance was consistently reached with a small number of subjects indicating the effect size was sufficiently large to be consistently detected anyway. Adding more subjects would therefore serve to increase significance of the relationship between barley and lower blood cholesterol or to narrow the confidence interval in favor of barley. FSANZ's conclusion is therefore not justified by any data or statements made in the scientific review.

The following are excerpts from the Science Review entitled "*Supporting document 1 Systematic Review of the Evidence for a Relationship between Oats, Barley and their derived β-glucans on Blood Cholesterol Concentration*" demonstrate consistent outcomes in human trials and high levels of significance for those findings. Please see Appendix for specific data from the scientific review that supports the inclusion of barley into the high level and general level health claims.

The mechanistic evidence has been supportive of the role of soluble fiber, including beta-glucans, to decrease total and LDL-cholesterol. Discounting the importance of beta-glucan and to suggest dissociating the role of beta-glucans from the effect of oats and barley may have unintended consequences, including lower intakes of soluble fiber in the diet. Food manufacturers have sought higher beta-glucan and fiber content in their foods to appeal to consumers that seek health benefits, including the reduction of cardiovascular health risk. Use of these high level health claims based on the beta-glucan in oats and barley have incentivized the food industry to increase higher oat and barley offerings and increase dietary intake. It is unknown what impact withdrawing the HLHC may have on whole grain oat and barley beta-glucan fiber intakes.

General Mills proposes that FSANZ clarify the HLHC relationship with minor changes to the claim language that include whole grain oats, oat bran, and whole grain barley. For example,

> "*whole grain oats [Oat bran, Barley] help(s) to reduce cholesterol concentrations in the blood and reduce risk of cardiovascular disease"*

FSANZ has indicated there is insufficient evidence to attribute the benefit solely to beta-glucan. Use of the descriptor 'whole grain oats - ' or 'whole grain barley beta-glucan' would address this gap. In addition, this proposal helps acknowledge the consistent opinion of experts and plethora of scientific evidence that beta-glucan is the most plausible mechanism and is a common thread between oats and barley research to reduce blood cholesterol.

FSANZ's consultation paper based the withdrawl of support for beta-glucan on the principal that no pure beta-glucan research exists that would unequivocally prove beta-glucan is the primary effector in reducing cholesterol. General Mills believes the scientific standard being applied by FSANZ in regard to beta-glucan, and barley, is not reasonable for foods. The ability to establish undisputable causal relationships between dietary factors found in whole foods in the same manner as purified pharmacological agents is an impossible standard.
As acknowledged in the review, isolation of beta-glucan from highly enriched grains, like barley, is challenging. Enrichment requires enzymatic hydrolysis and centrifugation to achieve even 70% purity, one of the highest concentrations of beta-glucan in an ingredient developed to date. .
The steps necessary to achieve relative purity of 100% beta-glucan is likely to modify the composition of the fiber (decrease molecular weight) so that the product would no longer represent the fiber as found in the food. Therefore, evaluating efficacy of a pure beta-glucan is unlikely to yield relevant results.

Regulatory Claim Compliance

General Mills requests that FSANZ retain beta-glucan as the compliance marker for use of the high level and general level health claims regardless of whether they withdraw use of beta-glucan outside of the oat and barley context

Although the scientific review was unable to identify research examining pure beta-glucan to assess the impact on health endpoints, the role of beta-glucan as a viscous soluble fiber makes it the most likely contributor to the observed effect. Research has conclusively shown that a minimum amount of beta-glucan is present in the oat and barley to elicit an effect (i.e., 3 grams per day). As a result, a minimum beta-glucan content in a food serving has been the standard upon which the health claim is based – in Australia, the EU and the USA at between 0.75 and 1 gram per serving. Even if evidence is insufficient to describe the effector of oats and barley as

'beta-glucan', it does not negate the importance of retaining a minimum threshold of beta-glucan for health claims based on considerable scientific agreement.

Research published after December 2014 Systematic Review inclusion date

The following research papers have publication dates after the final cut-off from the Scientific Review (i.e., post December 2014). In summary, these papers constitute more reviews that conclude the effect of barley and oat beta-glucan is to reduce blood cholesterol and reduce health risks.

i. Ho HV, Sievenpiper JL, Zurbau A, Mejia SB, Jovanovski E, Au-Yeung F, Jenkins AL, Vuksan V. A systematic review and meta-analysis of randomized controlled trials of the effect of barley β-glucan on LDL-C, non-HDL-C and apoB for cardiovascular disease risk reduction. Eur J Clin Nutr. 2016 Nov;70(11):1239-1245.
ii. Ho HV, Sievenpiper JL, Zurbau A, Blanco Mejia S, Jovanovski E, Au-Yeung F, Jenkins AL, Vuksan V. The effect of oat β-glucan on LDL-cholesterol, non-HDL-cholesterol and apoB for CVD risk reduction: a systematic review and meta-analysis of randomised-controlled trials. Br J Nutr. 2016 Oct;116(8):1369-1382.
iii. Zhu X, Sun X, Wang M, Zhang C, Cao Y, Mo G, Liang J, Zhu S. Quantitative assessment of the effects of beta-glucan consumption on serum lipid profile and glucose level in hypercholesterolemic subjects. Nutr Metab Cardiovasc Dis. 2015 Aug;25(8):714-23.
iv. Wang Y, Ames NP, Tun HM, Tosh SM, Jones PJ, Khafipour E. High Molecular Weight Barley β-Glucan Alters Gut Microbiota Toward Reduced Cardiovascular Disease Risk. Front Microbiol. 2016 Feb 10;7:129.

FSANZ sought input regarding the potential business impact of proposed changes to the HLHC. General Mills and Nestlé have a joint venture, Cereal Partners Worldwide (CPW), that produces and sells ready-to-eat breakfast cereals that include significant amounts of whole grains in Australia and New Zealand. The following are potential impacts to this business if FSANZ were to modify the current HLHC and GLHC.

1) Changes to packaging and label would be required on all products currently making claims about beta-glucan and blood cholesterol, to change the reference to oats instead, and to remove the dietary context statement. Modification to packaging and labels is also resource intensive and requires extensive lead times

2) FSANZ needs to determine whether a new dietary context statement will take the place of what currently exists. Will the proposed changes be limited to criteria that maintains parts of the health claim or will additional criteria be introduced? Without more detail regarding

the proposed changes, it is not possible to comment exhaustively on the impacts to the business.

Respectfully submitted,

Kevin Miller, PhD
Principal Scientist, Global Scientific and Regulatory Affairs
Bell Institute of Health and Nutrition
General Mills, Inc.
One General Mills Blvd
Minneapolis, MN 55426
[redacted]

APPENDIX

a. Figure 9 (page 22) forest plot shows that the effect of barley on total cholesterol was consistently favorable and also significant. Increasing the number of subjects would influence significance, but not change direction of the relationship.

Consumption of barley resulted in a significant change in total cholesterol (-0.32 mmol/L, 95% CI: -0.42, -0.21, *P*<0.00001, Figure 9). Heterogeneity, as indicated by I^2, was low at 40%.

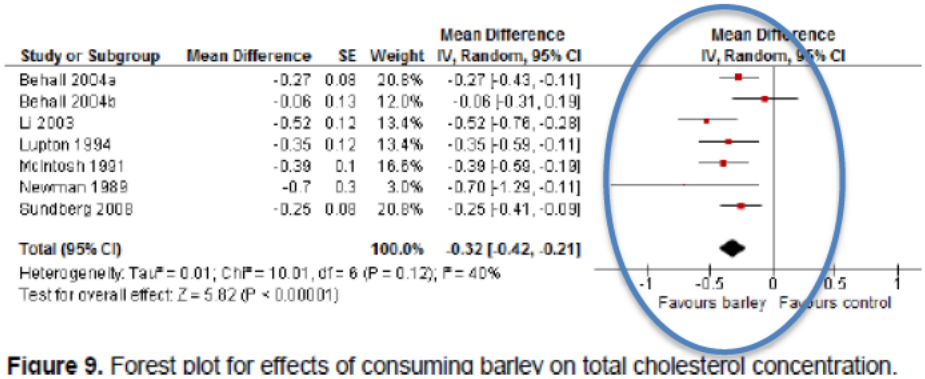

Figure 9. Forest plot for effects of consuming barley on total cholesterol concentration.

b. Figure 10 (page 22) forest plot also shows a consistently favorable effect of barley on LDL-cholesterol reduction that was reported as highly significant (P < 0.00001).

Intake of barley reduced LDL cholesterol significantly (-0.25 mmol/L; 95% CI: -0.32, -0.18, *P*<0.00001, Figure 10). There was no important heterogeneity (I^2 = 12%) which means that variation among study results can be attributed to chance.

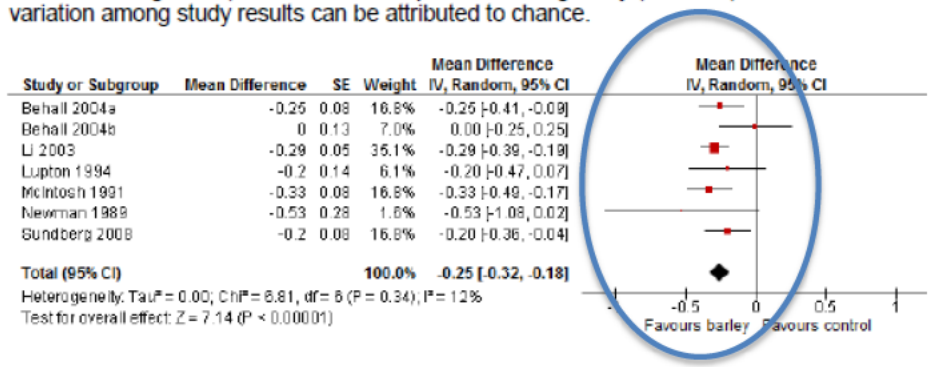

Figure 10. Forest plot for effects of consuming barley on LDL cholesterol concentration.

c. Table 4 (page 24) reports statistical significance for barley in the reduction of both total and LDL cholesterol

Table 4: *Results of sub-group analyses for total, LDL and HDL cholesterol concentration changes using random effects model from studies assessing the relationship between consumption of barley and blood cholesterol concentration*

Sub-group		No. strata	Total cholesterol Mean difference (95% CI)	*P*	Total cholesterol *P*-value Sub-group difference	LDL cholesterol Mean difference (95% CI)	*P*	LDL cholesterol *P*-value Sub-group difference	HDL cholesterol Mean difference (95% CI)	*P*	HDL cholesterol *P*-value Sub-group difference
Overall		7	-0.32 [-0.42, -0.21] I^2 = 40%	<0.00001	n/a	-0.25 [-0.32, -0.18] I^2 = 12%	<0.00001	n/a	-0.03 [-0.06, 0.00] I^2 = 0%	0.49	n/a
Baseline total cholesterol	<5.5	2	-0.54 [-0.76, -0.33] I^2 = 0%	<0.00001	0.02	-0.30 [-0.39, -0.20] I^2 = 0%	<0.00001	0.28	-0.08 [-0.18, 0.02] I^2 =0%	0.12	0.27
	≥5.5	5	-0.27 [-0.36, -0.18] I^2 = 12%	<0.00001		-0.22 [-0.32, -0.13] I^2 = 19%	<0.00001		-0.02 [-0.05, 0.01] I^2 = 2%	0.49	
Study quality	High	2	-0.38 [-0.78, 0.02] I^2 = 52%	0.06	0.78	-0.26 [-0.50, -0.01] I^2 = 22%	0.04	0.99	-0.05 [-0.11, 0.00] I^2 = 0%	0.06	0.24
	Low	5	-0.32 [-0.45, -0.19] I^2 = 48%	<0.00001		-0.25 [-0.34, -0.17] I^2 = 25%	<0.00001		-0.02 [-0.05, 0.02] I^2 = 0%	0.49	

n/a not applicable