EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to -hydroxy -methylbutyrate monohydrate (HMB) alone or in combination with -ketoisocaproic acid (KIC) and reduction of muscle tissue damage during exercise (ID 1577, 1584), increase in lean body mass (ID 1579, 1582, 1583), increase in muscle strength (ID 1578, 1583, 1587), increase in endurance performance (ID 1580, 1581), skeletal muscle tissue repair (ID 1586) and faster recovery from muscle fatigue after exercise (ID 1576, 1585) pursuant to Article 13(1) of Regulation (EC) No 1924/2006

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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to β-hydroxy β-methylbutyrate monohydrate (HMB) alone or in combination with α-ketoisocaproic acid (KIC) and reduction of muscle tissue damage during exercise (ID 1577, 1584), increase in lean body mass (ID 1579, 1582, 1583), increase in muscle strength (ID 1578, 1583, 1587), increase in endurance performance (ID 1580, 1581), skeletal muscle tissue repair (ID 1586) and faster recovery from muscle fatigue after exercise (ID 1576, 1585) pursuant to Article 13(1) of Regulation (EC) No 1924/2006[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to β-hydroxy β-methylbutyrate monohydrate (HMB) alone or in combination with α-ketoisocaproic acid (KIC) and reduction of muscle tissue damage during exercise, increase in lean body mass, increase in muscle strength, increase in endurance performance, skeletal muscle tissue repair and faster recovery from muscle fatigue after exercise. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The food constituent that is the subject of the health claims is HMB, either alone or in combination with KIC. The Panel considers that HMB either alone or in combination with KIC is sufficiently characterised.

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[1] On request from the European Commission, Question No EFSA-Q-2008-2313, EFSA-Q-2008-2314, EFSA-Q-2008-2315, EFSA-Q-2008-2316, EFSA-Q-2008-2317, EFSA-Q-2008-2318, EFSA-Q-2008-2319, EFSA-Q-2008-2320, EFSA-Q-2008-2321, EFSA-Q-2008-2322, EFSA-Q-2008-2323, EFSA-Q-2008-2324, adopted on 08 April 2011.

[2] Panel members: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Monika Neuhäuser-Berthold, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Daniel Tomé, Hendrik van Loveren and Hans Verhagen. Correspondence: nda@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank for the preparatory work on this scientific opinion: The members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren and Hans Verhagen. The members of the Claims Sub-Working Group on Weight Management/Satiety/Glucose and Insulin Control/Physical Performance: Kees de Graaf, Joanne Harrold, Mette Hansen, Mette Kristensen, Anders Sjödin and Inge Tetens.

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Reduction of muscle tissue damage during exercise

The claimed effects are "minimize muscle protein breakdown" and "HMB and exercise induced muscle breakdown". The target population is assumed to be adults performing resistance exercise. In the context of the proposed wordings and the references provided, the Panel assumes that the claimed effects relate to the reduction of damage to muscle tissue during exercise. The Panel considers that reduction of muscle tissue damage during exercise is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that although one small randomised controlled trial with methodological limitations reported a significant effect of HMB in combination with KIC on surrogate measures of muscle damage during resistance training, one meta-analysis of randomised controlled trials, which included five studies and eight intervention arms, did not show an effect of HMB supplementation on muscle tissue damage during exercise.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and reduction of muscle tissue damage during exercise.

Increase in lean body mass

The claimed effects are "increasing mass", "HMB and lean body mass", and "HMB and training adaptations". The target population is assumed to be physically active individuals in the general population. In the context of the proposed wordings, the Panel assumes that the claimed effects refer to an increase in lean body mass relative to body fat mass. The Panel considers that an increase in lean body mass is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that a meta-analysis of ten randomised controlled trials, and one additional randomised controlled trial not included in the meta-analysis, did not show a significant effect of HMB consumption on lean body mass during training compared to placebo.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in lean body mass.

Increase in muscle strength

The claimed effects are "increasing strength", "HMB and training adaptations", and "HMB and changes in muscle strength during training". The target population is assumed to be adults performing resistance training to improve muscle strength. In the context of the proposed wordings, the Panel assumes that the claimed effects refer to an increase in muscle strength. The Panel considers that an increase in muscle strength is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that the results from a meta-analysis of randomised controlled trials with respect to the effect of HMB consumption on muscle strength are inconsistent, that no significant effect of HMB consumption on muscle strength was shown in the target population for the claim, and that no evidence for a mechanism by which HMB could exert the claimed effect was provided.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in muscle strength.

Increase in endurance performance

The claimed effects are "increasing exercise lactate threshold and VO_2 peak", and "HMB and aerobic metabolism". The target population is assumed to be adults performing endurance exercise. In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effects refer to an increase in endurance performance. The Panel considers that increase in endurance performance is a beneficial physiological effect.

No references which addressed the effects of HMB supplementation in humans on measures of endurance performance, and from which conclusions could be drawn for the scientific substantiation of the claim, were provided.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in endurance performance.

Skeletal muscle tissue repair

The claimed effect is "HMB and normal muscle repair". The target population is assumed to be adults performing resistance exercise. In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the rebuilding of structural protein within skeletal muscle tissue after exercise which has caused muscle damage. The Panel considers that skeletal muscle tissue repair is a beneficial physiological effect.

No references which addressed the effects of HMB supplementation in humans on measures of skeletal muscle tissue repair were provided.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and skeletal muscle tissue repair.

Faster recovery from muscle fatigue after exercise

The claimed effects are "sport exercise recovery" and "HMB and muscle recovery after training". The target population is assumed to be adults performing strenuous exercise. The Panel assumes that the claimed effects refer to muscle fatigue recovery after exercise. The Panel considers that faster recovery from muscle fatigue after exercise is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that the one human intervention study provided from which conclusions could be drawn for the scientific substantiation of the claim did not show an effect of HMB on faster recovery from muscle fatigue after exercise.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and faster recovery from muscle fatigue after exercise.

KEY WORDS

β-hydroxy β-methylbutyrate monohydrate, α-ketoisocaproic acid, HMB, KIC, muscle, strength, endurance, repair, exercise, health claims.

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INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation EC (No) 1924/2006[4] submitted by Member States contains main entry claims with corresponding conditions of use and literature for similar health claims. EFSA has screened all health claims contained in the original consolidated list of Article 13 health claims which was received by EFSA in 2008 using six criteria established by the NDA Panel to identify claims for which EFSA considered sufficient information had been provided for evaluation and those for which more information or clarification was needed before evaluation could be carried out[5]. The clarifications which were received by EFSA through the screening process have been included in the consolidated list. This additional information will serve as clarification to the originally provided information. The information provided in the consolidated list for the health claims which are the subject of this opinion is tabulated in Appendix C.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claims is "HMB (β-hydroxy β-methylbutyrate monohydrate)" and "HMB and HMB/KIC combinations".

From the information provided, the Panel assumes that the food constituent that is the subject of the health claims is HMB, either alone or in combination with α-ketoisocaproic acid (KIC).

β-Hydroxy β-methylbutyric acid (HMB), or β-hydroxy β-methylbutyrate, is a metabolite of the amino acid leucine. HMB can be synthesised in the human body (about 0.2-0.4 g/day) and is usually available in supplements as a calcium salt. KIC is also an intermediate metabolite of leucine. Both HMB and KIC can be measured in food by established methods.

The Panel considers that the food constituent, either HMB alone or in combination with KIC, which is the subject of the health claims, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Reduction of muscle tissue damage during exercise (ID 1577, 1584)

The claimed effects are "minimize muscle protein breakdown" and "HMB and exercise induced muscle breakdown". The Panel assumes that the target population is adults performing resistance exercise.

In the context of the proposed wordings and the references provided, the Panel assumes that the claimed effects relate to the reduction of damage to muscle tissue during exercise.

The Panel considers that reduction of muscle tissue damage during exercise is a beneficial physiological effect.

[4] Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

[5] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. EFSA Journal, 9(4):2135, 24 pp.

2.2. Increase in lean body mass (ID 1579, 1582, 1583)

The claimed effects are "increasing mass", "HMB and lean body mass", and "HMB and training adaptations". The Panel assumes that the target population is physically active individuals in the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effects refer to an increase in lean body mass relative to body fat mass.

The Panel considers that an increase in lean body mass is a beneficial physiological effect.

2.3. Increase in muscle strength (ID 1578, 1583, 1587)

The claimed effects are "increasing strength", "HMB and training adaptations", and "HMB and changes in muscle strength during training". The Panel assumes that the target population is adults performing resistance training to improve muscle strength.

In the context of the proposed wordings, the Panel assumes that the claimed effects refer to an increase in muscle strength. In sports, muscle strength is sometimes a limiting factor for physical performance.

The Panel considers that an increase in muscle strength is a beneficial physiological effect.

2.4. Increase in endurance performance (ID 1580, 1581)

The claimed effects are "increasing exercise lactate threshold and VO_2 peak", and "HMB and aerobic metabolism". The Panel assumes that the target population is adults performing endurance exercise.

In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effects refer to an increase in endurance performance. Endurance performance relates to the ability to complete certain tasks with higher intensity, faster, or with a higher power output when performing long-term exercise.

The Panel considers that an increase in endurance performance is a beneficial physiological effect.

2.5. Skeletal muscle tissue repair (ID 1586)

The claimed effect is "HMB and normal muscle repair". The Panel assumes that the target population is adults performing resistance exercise.

In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the rebuilding of structural protein within skeletal muscle tissue after exercise which has caused muscle damage.

The Panel considers that skeletal muscle tissue repair is a beneficial physiological effect.

2.6. Faster recovery from muscle fatigue after exercise (ID 1576, 1585)

The claimed effects are "sport exercise recovery" and "HMB and muscle recovery after training". The Panel assumes that the target population is adults performing strenuous exercise.

The Panel assumes that the claimed effects refer to muscle fatigue recovery after exercise.

Fatigue can be defined as the loss of peak force or power output. Therefore, muscle fatigue recovery can be defined as the regain of maximal muscle strength or muscle power after performance of strenuous exercise which has induced muscle fatigue.

The Panel considers that faster recovery from muscle fatigue after exercise is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

Some of the references provided for the scientific substantiation of the claims evaluated in this opinion were studies and narrative reviews which addressed the effects of HMB on outcomes (e.g. fat metabolism, hepatic and renal function, and cardiovascular system function) unrelated to the claimed effects, or which did not include original data for the scientific substantiation of the claim. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claims.

A meta-analysis of randomised controlled trials (RCTs) (Rowlands and Thomson, 2009) on the effects of HMB on outcomes of body composition, muscle strength and muscle damage included the majority of the publications submitted, and from which conclusions could be drawn for the scientific substantiation of the claims. The meta-analysis included 10 RCTs with a parallel design and one RCT with a cross-over design (with one-week washout between interventions). In these trials (17 intervention arms), 12 intervention arms assessed measures of muscle strength, 16 intervention arms provided body composition estimates, and eight intervention arms reported on muscle damage assessed by creatine kinase (CK) concentrations. The meta-analysis comprised 394 trained (n=259) and untrained (n=135) weight lifters on resistance training for 5±6 h/week (range 3-20 h/week), and interventions lasting 3-9 weeks. The HMB dose in all but two studies was 3.0 g/day (range 1.5-6.0 g/day).

Another meta-analysis of RCTs on the effects of HMB supplementation on lean body mass and strength during resistance training, and which included a literature search from 1967 to 2001, was provided (Nissen and Sharp, 2003). This meta-analysis included only seven RCTs on HMB (and 9 intervention arms), all of which were included in the meta-analysis by Rowlands and Thomson (2009). The Panel considers that this meta-analysis does not provide evidence for the scientific substantiation of the claims in addition to that of the meta-analysis by Rowlands and Thomson (2009).

3.1. Reduction of muscle tissue damage during exercise (ID 1577, 1584)

In the meta-analysis by Rowlands and Thomson (2009), a total of five studies, including eight effect estimates, addressed the effects of HMB supplementation on muscle damage during resistance training by means of blood concentrations of CK as a marker of muscle membrane damage (Jówko et al., 2001; Kreider et al., 1999; Kreider et al., 2000; Nissen et al., 1996; Panton et al., 2000). All intervention arms used doses of HMB of 3.0 g/day except one (i.e. 1.5 g/day). Five arms used untrained subjects whereas three used trained subjects. All subjects were young males (87 in the intervention and 88 in the control group). No significant effect of HMB consumption on CK concentrations was observed compared to placebo.

Two studies, which addressed the effect of HMB on measures of muscle damage, and which were not included in the meta-analysis, were also provided (Knitter et al., 2000; van Someren et al., 2005).

In the cross-over RCT by van Someren et al. (2005), six non resistance trained male subjects performed an exercise protocol designed to induce muscle damage on the dominant or non-dominant arm on two separate occasions. Subjects consumed HMB in combination with KIC (3.0 g HMB and 0.3 g KIC, daily) and placebo (3.0 g corn flour) given in three equal doses during the day, for 14 days

prior to exercise. The order of the interventions was randomised. One repetition maximum (1RM), plasma CK activity, delayed onset muscle soreness (DOMS), limb girth, and range of motion (ROM) were determined pre-exercise, at 1 h, 24 h, 48 h, and 72 h post-exercise. The Panel notes that the primary outcome of the study was not identified, that no power calculations were performed, and that no control for multiplicity of analyses was applied. HMB and KIC supplementation significantly attenuated the CK response compared to placebo ($p<0.05$). The Panel considers that limited conclusions can be drawn from this study for the scientific substantiation of the claim.

In the RCT by Knitter et al. (2000), subjects (n=16, 8 males) were paired according to their 2-mile run times and past running experience. Each pair was randomly assigned a treatment of either HMB (3.0 g/day) or placebo (rice maltodextrin). After six weeks of daily training and supplementation, all subjects participated in a prolonged run (20-km course). CK and lactate dehydrogenase (LDH) activities were measured before and after the run to assess muscle damage. Three subjects from the placebo group withdrew from the study, and data analyses were performed in the sample of completers only (n=5 placebo, n=8 HMB). Power calculations were not performed. The Panel notes that all drop outs belonged to the placebo group, and that drop outs (and therefore the breaking of the initial group matching by training status) were not taken into account in data analysis. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

In weighing the evidence, the Panel took into account that although one small RCT with methodological limitations reported a significant effect of HMB in combination with KIC on surrogate measures of muscle damage during resistance training, one meta-analysis of RCTs which included five studies and eight intervention arms did not show an effect of HMB supplementation on muscle tissue damage during exercise.

The Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and reduction of muscle tissue damage during exercise.

3.2. Increase in lean body mass (ID 1579, 1582, 1583)

Ten of the 11 RCTs considered in the meta-analysis by Rowlands and Thomson (2009), and which included 16 intervention arms, assessed the effects of HMB supplementation on lean body mass and reported size estimates. Body composition was assessed by skin fold thickness in three trials (Gallagher et al., 2000; Panton et al., 2000; Ransone et al., 2003), by bioelectrical impedance analysis (BIA) in two trials (Jówko et al., 2001; Thomson et al., 2009), by total body electrical conductivity (TOBEC) in one trial (Nissen et al., 1996), and by dual-energy x-ray absorptiometry (DXA) in four trials (Kreider et al., 1999; Kreider et al., 2000; Slater et al., 2001; Vukovich et al., 2001). No significant effect of HMB on changes in fat-free mass was observed in either trained (mean=0.8 %, 90 % CI -0.4 % to 2 %) or untrained (mean=0.9 %, 90 % CI -0.2 % to 2 %) subjects. The Panel notes that skin fold thickness, BIA and TOBEC may not be as reliable methods as DXA to assess changes in body composition in short-term intervention studies. The Panel also notes that none of the studies which assessed changes in lean body mass using DXA found a significant effect of HMB compared to placebo.

An additional RCT, which assessed the effects of HMB supplementation on lean body mass and which was not included in the meta-analysis by Rowlands and Thomson (2009), was provided (Lamboley et al., 2007). College students were randomly assigned to consume either HMB (3 g/day; n=8, 4 men) or placebo (placebo not reported; n=8, 4 men) for a 5-week supplementation period during which they underwent interval training three times a week on a treadmill. Body composition was assessed by DXA before and after training. No significant differences between groups were observed with respect to changes in body composition, including lean body mass.

In weighing the evidence, the Panel took into account that a meta-analysis of ten RCTs, and one additional RCT not included in the meta-analysis, did not show a significant effect of HMB consumption on lean body mass during training compared to placebo.

The Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in lean body mass.

3.3. Increase in muscle strength (ID 1578, 1583, 1587)

Ten of the 11 RCTs considered in the meta-analysis by Rowlands and Thomson (2009), and which included 14 intervention arms, assessed the effects of HMB supplementation on measures of overall, upper and lower body muscular strength. The strength measure used was 1RM in seven studies (Gallagher et al., 2000; Jówko et al., 2001; Kreider et al., 1999; Panton et al., 2000; Ransone et al., 2003; Thomson et al., 2009; Vukovich and Dreifort, 2001), 3RM in two studies (O'Connor and Crowe, 2003; Slater et al., 2001) and a strength index, calculated as the average weight lifted to failure (4-6 repetitions) during three sets multiplied by the number of repetitions the weight was lifted, in one study (Nissen et al., 1996). There was a small but statistically significant effect of HMB on overall average muscle strength when all studies and subjects were combined (mean=3.7 %, 90 % CI 1.3 % to 6.1 %). This effect was due to the significant changes observed in untrained individuals (mean=6.6 %, 90 % CI 0.9 % to 2.3 %), particularly in lower body strength (mean=9.9 %, 90 % CI 4 % to 15.8 %). No significant changes in muscle strength were observed in the upper body for untrained lifters, or for trained lifters in overall, upper body or lower body strength. No explanation for the differential effects of HMB supplementation observed in trained *vs.* untrained subjects, or in upper *vs.* lower body strength in untrained subjects, has been provided. The Panel notes that the results from this meta-analysis with respect to the effect of HMB consumption on muscle strength are inconsistent. The Panel also notes that no significant effect of HMB consumption on muscle strength was shown in the target population (i.e. active individuals who are performing resistance training to improve muscle strength) for the claim.

An effect of HMB on protein turnover leading to an increase in lean body mass, and an effect of HMB on the reduction of skeletal muscle damage during exercise, have been hypothesised as the mechanisms by which HBM could improve muscle strength. However, the Panel notes that no evidence has been provided for any of these mechanisms (see sections 3.1 and 3.2).

In weighing the evidence, the Panel took into account that the results from a meta-analysis of RCTs with respect to the effect of HMB consumption on muscle strength are inconsistent, that no significant effect of HMB consumption on muscle strength was shown in the target population for the claim, and that no evidence for a mechanism by which HMB could exert the claimed effect was provided.

The Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in muscle strength.

3.4. Increase in endurance performance (ID 1580, 1581)

Two of the human intervention studies provided assessed the effects of HMB on measures of maximal oxygen consumption (VO_2 max), on ventilatory threshold or on the onset of blood lactate accumulation (Lamboley et al., 2007; Vukovich and Dreifort, 2001), but the studies did not include any measure of endurance performance. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

In a RCT by O'Connor and Crowe (2003), the effects of a 6-week oral supplementation with HMB (3.0 g/day) *vs.* a mixture of HMB and creatine monohydrate (3.0 g/day HMB plus 3.0 g/day creatine) on aerobic and anaerobic capacity, peak power and total work during a cycling test in highly trained

rugby players were assessed. The control group was self-selected and received no treatment. The Panel notes that randomisation and blinding were only applied to subjects assigned to the two intervention groups. No statistically significant effect of HMB on peak power or total work was observed compared to the control group. The Panel notes the important limitations of the study design, and considers that no conclusions can be drawn for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in endurance performance.

3.5. Skeletal muscle tissue repair (ID 1586)

No references addressing the effects of HMB supplementation in humans on measures of skeletal muscle tissue repair were provided.

The Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and skeletal muscle tissue repair.

3.6. Faster recovery from muscle fatigue after exercise (ID 1576, 1585)

In the RCT by Paddon-Jones et al. (2001), non resistance trained male subjects were randomly assigned to consume 40 mg/kg body weight per day of HMB (n=8) or placebo (maltodextrin calcium carbonate, n=9) for six days prior to a bout of 24 maximal isokinetic eccentric contractions of the elbow flexors, and this protocol continued throughout post testing. Muscle soreness, upper arm girth, and torque measures were assessed pre-exercise, 15 min post-exercise, and 1, 2, 3, 4, 7, and 10 days post-exercise. Power calculations were not performed. No pre-test differences between HMB and control groups were observed, and both groups performed a similar amount of eccentric work during the main eccentric exercise bout. HMB supplementation had no effect on swelling, muscle soreness, or torque following the damaging eccentric exercise bout. The Panel notes that this study does not show an effect of HMB on faster recovery from muscle fatigue after exercise.

No other references which addressed the effects of HMB supplementation in humans on measures of muscle fatigue recovery after exercise were provided.

In weighing the evidence, the Panel took into account that the one human intervention study provided from which conclusions could be drawn for the scientific substantiation of the claim did not show an effect of HMB on faster recovery from muscle fatigue after exercise.

The Panel concludes that a cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and faster recovery from muscle fatigue after exercise.

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food constituent, HMB either alone or in combination with KIC, which is the subject of the health claims, is sufficiently characterised.

Reduction of muscle tissue damage during exercise (ID 1577, 1584)

- The claimed effects are "minimize muscle protein breakdown" and "HMB and exercise induced muscle breakdown". The target population is adults performing resistance exercise. Reduction of muscle tissue damage during exercise is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and reduction of muscle tissue damage during exercise.

Increase in lean body mass (ID 1579, 1582, 1583)

- The claimed effects are "increasing mass", "HMB and lean body mass", and "HMB and training adaptations". The target population is assumed to be physically active individuals in the general population. Increase in lean body mass is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in lean body mass.

Increase in muscle strength (ID 1578, 1583, 1587)

- The claimed effects are "increasing strength", "HMB and training adaptations", and "HMB and changes in muscle strength during training". The target population is assumed to be adults performing resistance training to improve muscle strength. Increase in muscle strength is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in muscle strength.

Increase in endurance performance (ID 1580, 1581)

- The claimed effects are "increasing exercise lactate threshold and VO_2 peak", and "HMB and aerobic metabolism". The target population is assumed to be adults performing endurance exercise. An increase in endurance performance is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and increase in endurance performance.

Skeletal muscle tissue repair (ID 1586)

- The claimed effect is "HMB and normal muscle repair". The target population is assumed to be adults performing resistance exercise. Skeletal muscle tissue repair is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and skeletal muscle tissue repair.

Faster recovery from muscle fatigue after exercise (ID 1576, 1585)

- The claimed effects are "sport exercise recovery" and "HMB and muscle recovery after training". The target population is assumed to be adults performing strenuous exercise. It is assumed that the claimed effects refer to muscle fatigue recovery after exercise. Faster recovery from muscle fatigue after exercise is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of HMB, either alone or in combination with KIC, and faster recovery from muscle fatigue.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-2313, EFSA-Q-2008-2314, EFSA-Q-2008-2315, EFSA-Q-2008-2316, EFSA-Q-2008-2317, EFSA-Q-2008-2318, EFSA-Q-2008-2319, EFSA-Q-2008-2320, EFSA-Q-2008-2321, EFSA-Q-2008-2322, EFSA-Q-2008-2323, EFSA-Q-2008-2324). The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The full list of supporting references as provided to EFSA is available on: http://www.efsa.europa.eu/panels/nda/claims/article13.htm.

REFERENCES

Gallagher PM, Carrithers JA, Godard MP, Schulze KE and Trappe SW, 2000. Beta-hydroxy-beta-methylbutyrate ingestion, part II: effects on hematology, hepatic and renal function. Medicine and Science in Sports and Exercise, 32, 2116-2119.

Jówko E, Ostaszewski P, Jank M, Sacharuk J, Zieniewicz A, Wilczak J and Nissen S, 2001. Creatine and beta-hydroxy-beta-methylbutyrate (HMB) additively increase lean body mass and muscle strength during a weight-training program. Nutrition, 17, 558-566.

Knitter AE, Panton L, Rathmacher JA, Petersen A and Sharp R, 2000. Effects of beta-hydroxy-beta-methylbutyrate on muscle damage after a prolonged run. Journal of Applied Physiology, 89, 1340-1344.

Kreider RB, Ferreira M, Wilson M and Almada AL, 1999. Effects of calcium beta-hydroxy-beta-methylbutyrate (HMB) supplementation during resistance-training on markers of catabolism, body composition and strength. International Journal of Sports Medicine, 20, 503-509.

Kreider RB, Ferreira M, Greenwood M, Wilson M, Grindstaff P, Plisk S, Reinardy J, Cantler E and Almada AL, 2000. Effects of Calcium β-HMB Supplementation During Training on Markers of Catabolism, Body Composition, Strength and Sprint Performance. Journal of Exercise Physiology online, 3, 48-59.

Lamboley CR, Royer D and Dionne IJ, 2007. Effects of beta-hydroxy-beta-methylbutyrate on aerobic-performance components and body composition in college students. International Journal of Sport Nutrition and Exercise Metabolism, 17, 56-69.

Nissen S, Sharp R, Ray M, Rathmacher JA, Rice D, Fuller JC, Jr., Connelly AS and Abumrad N, 1996. Effect of leucine metabolite beta-hydroxy-beta-methylbutyrate on muscle metabolism during resistance-exercise training. Journal of Applied Physiology, 81, 2095-2104.

Nissen SL and Sharp RL, 2003. Effect of dietary supplements on lean mass and strength gains with resistance exercise: a meta-analysis. Journal of Applied Physiology, 94, 651-659.

O'Connor DM and Crowe MJ, 2003. Effects of beta-hydroxy-beta-methylbutyrate and creatine monohydrate supplementation on the aerobic and anaerobic capacity of highly trained athletes. Journal of Sports Medicine and Physical Fitness, 43, 64-68.

Paddon-Jones D, Keech A and Jenkins D, 2001. Short-term beta-hydroxy-beta-methylbutyrate supplementation does not reduce symptoms of eccentric muscle damage. International Journal of Sport Nutrition and Exercise Metabolism, 11, 442-450.

Panton LB, Rathmacher JA, Baier S and Nissen S, 2000. Nutritional supplementation of the leucine metabolite beta-hydroxy-beta-methylbutyrate (HMB) during resistance training. Nutrition, 16, 734-739.

Ransone J, Neighbors K, Lefavi R and Chromiak J, 2003. The effect of beta-hydroxy beta-methylbutyrate on muscular strength and body composition in collegiate football players. Journal of Strength and Conditioning Research, 17, 34-39.

Rowlands DS and Thomson JS, 2009. Effects of [beta]-Hydroxy-[beta]-Methylbutyrate Supplementation During Resistance Training on Strength, Body Composition, and Muscle Damage in Trained and Untrained Young Men: A Meta-Analysis. Journal of Strength & Conditioning Research, 23, 836-846.

Slater G, Jenkins D, Logan P, Lee H, Vukovich M, Rathmacher JA and Hahn AG, 2001. Beta-hydroxy-beta-methylbutyrate (HMB) supplementation does not affect changes in strength or body composition during resistance training in trained men. International Journal of Sport Nutrition and Exercise Metabolism, 11, 384-396.

Thomson JS, Watson PE and Rowlands DS, 2009. Effects of nine weeks of β-hydroxy-β-methylbutyrate supplementation on strength and body composition in resistance trained men. Journal of Strength and Conditioning Research, 23, 827-835.

van Someren KA, Edwards AJ and Howatson G, 2005. Supplementation with beta-hydroxy-beta-methylbutyrate (HMB) and alpha-ketoisocaproic acid (KIC) reduces signs and symptoms of exercise-induced muscle damage in man. International Journal of Sport Nutrition and Exercise Metabolism, 15, 413-424.

Vukovich MD, Stubbs NB and Bohlken RM, 2001. Body composition in 70-year-old adults responds to dietary beta-hydroxy-beta-methylbutyrate similarly to that of young adults. Journal of Nutrition, 131, 2049-2052.

Vukovich MD and Dreifort GD, 2001. Effect of beta-hydroxy beta-methylbutyrate on the onset of blood lactate accumulation and V(O)(2) peak in endurance-trained cyclists. Journal of Strength and Conditioning Research, 15, 491-497.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods[6] (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined as "any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

a) the role of a nutrient or other substance in growth, development and the functions of the body; or

b) psychological and behavioural functions; or

c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

(i) based on generally accepted scientific evidence; and

(ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13 (1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD[7]

Foods are commonly involved in many different functions[8] of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

[6] OJ L12, 18/01/2007
[7] The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.
[8] The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

(a) the claimed effect of the food is beneficial for human health,

(b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),

(c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,

(d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to

describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.

- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.

- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.
- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.
- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.
- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.
- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.

APPENDIX C

Table 1. Main entry health claims related to β-hydroxy β-methylbutyrate monohydrate, either alone or in combination with α-ketoisocaproic acid, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
1576	HMB (B-hydroxy B-methylbutyrate monohydrate)	Support exercise recovery Clarification provided Muscle recovery: Decreases creatine phosphokinase and LDH response, showing HMB helps prevent exercise-induced muscle damage.	HMB helps to enhance muscle energetics and recuperation. HMB helps with muscle energetics and recuperation
	Conditions of use - The product must contain at least 1 gram HMB per serving Claim to be used for foods for active individuals		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1577	HMB (B-hydroxy B-methylbutyrate monohydrate)	Minimize muscle protein breakdown	HMB helps to reduce muscle protein breakdown following exercise Ingredient clinically shown to support protection of muscles from breakdown following exercise HMB helps to reduce exercise-induced muscle tissue breakdown.
	Conditions of use - The product must contain at least 1 gram HMB per serving Claim to be used for foods for active individuals		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1578	HMB (B- hydroxy B-methylbutyrate monohydrate)	Increasing strength	HMB supports strength HMB has been shown to increase strength. HMB has the ability to enhance muscular strength Ingredient clinically shown to help boost strength Boost muscular strength
	Conditions of use - The product must contain at least 1 gram HMB per serving Claim to be used for foods for active individuals		

ID	Food or Food constituent	Health Relationship	Proposed wording
1579	HMB (B-hydroxy B-methylbutyrate monohydrate)	Increasing Mass	Supplementing with HMB may help improve body composition HMB supports maintenance of lean muscle mass With proper diet and exercise, HMB can help support an increase in fat free mass. HMB has been shown to increase lean muscle mass
	Conditions of use - The product must contain at least 1 gram HMB per serving Claim to be used for foods for active individuals		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1580	HMB (B-hydroxy B-methylbutyrate monohydrate)	Increasing exercise lactate threshold and VO2 peak	HMB may help increase the onset of blood lactate accumulation and VO2 peak.
	Conditions of use - The product must contain at least 1 gram HMB per serving Claim to be used for foods for active individuals		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1581	HMB	HMB and aerobic metabolism Clarification provided HMB increases VO2 max to a greater extent than training alone when used in conjunction with a cardiovascular training programme	HMB supplementation aids aerobic metabolism in endurance athletes, such as cyclists and runners
	Conditions of use - Minimum of 3g per day for 2 weeks (3)		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1582	HMB	HMB and lean body mass	HMB can increase gains in lean body mass during resistance training
	Conditions of use - Minimum of 3g HMB per day for 2 weeks combined with resistance training (10)		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1583	HMB	HMB and training adaptations	HMB can improve body adaptation to intense training

		Clarification provided Body adaptation to training: Increase lean body mass and muscle strength during a weight-training program.	
	Conditions of use - Minimum of 1.5g per day 2 weeks (10)		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1584	HMB and HMB/KIC combinations	HMB and exercise induced muscle breakdown	HMB supplementation can reduce muscle breakdown after intense training. HMB reduces the loss of muscle proteins after intense training
	Conditions of use - Minimum of 3g per day HMB and 0.3g KIC daily for 2 weeks (1)		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1585	HMB and HMB/KIC combinations	HMB and muscle recovery after training	HMB supplementation supports muscle recovery after training
	Conditions of use - Minimum of 3g per day HMB and 0.3g KIC daily for 2 weeks (1)		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1586	HMB and HMB/KIC combinations	HMB and normal muscle repair	HMB supplementation maintains normal muscle repair after training
	Conditions of use - Minimum of 3g per day HMB and 0.3g KIC daily for 2 weeks (1)		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1587	HMB and HMB/KIC combinations	HMB and changes in muscle strength during training	HMB increases muscle strength when taken during a resistance training program.
	Conditions of use - Minimum of 3g per day HMB and 0.3g KIC daily for 2 weeks (1) taken in conjunction with resistance training.		

GLOSSARY AND ABBREVIATIONS

BIA	Bioelectrical impedance analysis
CK	Creatine kinase
DOMS	Delayed onset muscle soreness
DXA	Dual-energy x-ray absorptiometry
HMB	β-hydroxy β-methylbutyric acid
KIC	α-ketoisocaproic acid
LDH	Lactate dehydrogenase
RCT	Randomised controlled trial
RM	Repetition maximum
ROM	Range of motion
TOBEC	Total body electrical conductivity