

## Manuscript Clarification

### Changes in body composition and performance with supplemental HMB-FA+ATP

Stuart M. Phillips, Ph.D., McMaster University

Alan A. Aragon, M.S., California State University, Northridge

Paul J. Arciero, Ph.D., Skidmore College

Shawn M. Arent, Ph.D., Rutgers University

Graeme L. Close, Ph.D., Liverpool John Moores University

D. Lee Hamilton, Ph.D., University of Stirling

Eric R. Helms, M.S., M.Phil, Sports Performance Research Institute New Zealand

Menno Henselmans, M.Sc., Bayesian Bodybuilding Research and Development

Jeremy P. Loenneke, Ph.D., The University of Mississippi

Layne E. Norton, Ph.D., BioLayne LLC

Michael J. Ormsbee, Ph.D., Florida State University

Craig Sale, Ph.D., Nottingham-Trent University

Brad J. Schoenfeld, Ph.D., Lehman College

Abbie E. Smith-Ryan Ph.D., University of North Carolina

Kevin D. Tipton, Ph.D., University of Stirling

Matthew D. Vukovich, Ph.D., South Dakota State University

Colin Wilborn, Ph.D., University of Mary Hardin-Baylor

Darryn S. Willoughby, Ph.D. Baylor University

---

### **Response from the Authors**

#### ***In response***

The authors are satisfied that their original responses to the prior Manuscript Clarification address the issues raised here.

Lowery et al. (6) reported, in contrast to an often-observed heterogeneity in training-induced

hypertrophy, remarkably consistent between-group changes in muscle mass to find statistical

significance between an HMB-FA+AP supplemented (n=8) versus a placebo (n=9) groups. The

difference divergence between the supplemented and placebo groups occurred despite optimal training and optimal nutritional support. We note that HMB has been shown to result in a trivial

training-induced adaptive advantage (8) and that the gain in lean body mass was in previously

resistance-trained subjects who would have had less propensity to gain lean body mass (7). For

absolute clarity, could the authors please present the absolute body weight and body composition (lean body mass and fat mass) as opposed to % change data? We believe this would be helpful for readers. There are data for calcium HMB showing improved muscle protein turnover (9). We

are unaware of any similar data for FA-HMB despite greater bioavailability and uptake (into

what tissue is unknown) (3). Do the authors know of any data showing that HMB-FA affects

human muscle protein turnover (9)? We note that leucine had the same anabolic effects as

calcium-HMB (9) and that dietary protein can exert a positive effect on gains in muscle mass

with resistance training (1). The placebo group, recipients of optimal protein/leucine intake, did not appear to respond at all to the overreaching phase. Can the authors speculate why? Lowery et al (6) supplemented with ATP, which has undetectable bioavailability (2). Wilson et al. (10), reported that ATP (400mg/d) resulted in a positive effect on muscle mass, strength, and power

gains. The authors' state (4) that a previously reported increase in post-exercise blood flow

induced by the ATP (5) in the supplemented group could be responsible. The magnitude of that

flow increase was only about 100-150 ml/min, was not consistently observed across weeks of

supplementation, and lasted no more than 3-6min post-exercise (5). How do the authors think a

small, inconsistent, and short-lasting increase in blood flow could affect performance? In the

response to Hyde et al (4), Lowery et al. (6) stated that they selected "...a responsive population who possess a quantity of lean mass indicative of previous responses to resistance training..." What was the screening process to pick the participants? The authors state their subjects had

muscle "...an order of magnitude [an order of magnitude is defined as 10-times greater, so this

cannot be the case] higher than average lean mass..." Could the authors please state the exact criteria for inclusion as a participant? It would be useful for the authors to describe how many participants were recruited and screened, the final number entered into the study and the number of dropouts. Were participants randomized to treatment and placebo groups, pair matched based on body mass, lean body mass, strength or another variable?

#### **Reference List**

1. Cermak NM, Res PT, de Groot LC, Saris WH and van Loon LJ. Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training: a

meta-analysis. *Am J Clin Nutr* 96: 1454-1464, 2012.

2. Coolen EJ, Arts IC, Bekers O, Vervaet C, Bast A and Dagnelie PC. Oral bioavailability of

ATP after prolonged administration. *Br J Nutr* 105: 357-366, 2011.

3. Fuller JC, Jr., Sharp RL, Angus HF, Baier SM and Rathmacher JA. Free acid gel form of betahydroxy- beta-methylbutyrate (HMB) improves HMB clearance from plasma in human subjects compared with the calcium HMB salt. *Br J Nutr* 105: 367-372, 2011.

4. Hyde PN, Kendall KL and LaFountain RA. Interaction of beta-hydroxy-beta-methylbutyrate free acid and adenosine triphosphate on muscle mass, strength, and power, in resistance trained individuals. *J Strength Cond Res* 30: e10-e14, 2016.

5. Jager R, Roberts MD, Lowery RP, Joy JM, Cruthirds CL, Lockwood CM, Rathmacher JA, Purpura M and Wilson JM. Oral adenosine-5'-triphosphate (ATP) administration increases blood flow following exercise in animals and humans. *J Int Soc Sports Nutr* 11: 28, 2014.

6. Lowery RP, Joy JM, Rathmacher JA, Baier SM, Fuller JC, Jr., Shelley MC, Jager R, Purpura M, Wilson SM and Wilson JM. Interaction of Beta-Hydroxy-Beta-Methylbutyrate Free Acid and Adenosine Triphosphate on Muscle Mass, Strength, and Power in Resistance Trained Individuals. *J Strength Cond Res* 30: 1843-1854, 2016.

7. Morton RW, Oikawa SY, Wavell CG, Mazara N, McGlory C, Quadriatero J, Baechler BL, Baker SK and Phillips SM. Neither load nor systemic hormones determine resistance

training-mediated hypertrophy or strength gains in resistance-trained young men. *J Appl Physiol*

(1985) 121: 129- 138, 2016.

8. Rowlands DS and Thomson JS. 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. *J Strength Cond Res* 23: 836-846, 2009.

9. Wilkinson DJ, Hossain T, Hill DS, Phillips BE, Crossland H, Williams J, Loughna P, Churchward-Venne TA, Breen L, Phillips SM, Etheridge T, Rathmacher JA, Smith K, Szewczyk

NJ and Atherton PJ. Effects of leucine and its metabolite beta-hydroxy-beta-methylbutyrate on human skeletal muscle protein metabolism. *J Physiol* 591: 2911-2923, 2013.

10. Wilson JM, Joy JM, Lowery RP, Roberts MD, Lockwood CM, Manninen AH, Fuller JC, De Souza EO, Baier SM, Wilson SM and Rathmacher JA. Effects of oral adenosine-5'-triphosphate

supplementation on athletic performance, skeletal muscle hypertrophy and recovery in resistance-trained men. *Nutr Metab (Lond)* 10: 57, 2013.

11. Wilson JM, Lowery RP, Joy JM, Andersen JC, Wilson SM, Stout JR, Duncan N, Fuller JC, Baier SM, Naimo MA and Rathmacher J. The effects of 12 weeks of beta-hydroxy-beta-methylbutyrate free acid supplementation on muscle mass, strength, and power in resistance-trained individuals: a randomized, double-blind, placebo-controlled study.

*Eur J Appl Physiol* 114: 1217-1227, 2014.

ACCEPTED