

From: Richard Cohen MD

To: ALR Industries Attention Author L. Rea

Subject: Preliminary observations of plasma amino acid ratios from fasted administration of 56g whey protein vs. 10 tablets x 4 HumaPro.

Date: August 1<sup>st</sup> 2011

Comparing both rate of appearance of plasma levels of amino acids, it appears that interindividual differences exist substantially in the whey supplementation group. Due to whey's complex biochemical structure, it requires several factors to break it down into its amino acids building blocks. These factors include: digestive enzymes, competition for uptake (due to formulation ratio of amino acids), and transport proteins that differ significantly between individuals. This explains the large inter-individual differences found in the whey group. For example, if we compare the Tryptophan changes in plasma in whey supplemented subjects, we observe a large difference between subjects:

Patient D: had an increase of 39.24 % while Patient C had an increase of 3 % - a difference of approximately 36 %.

On the other hand Patient D had an increase of 14 % while patient C had an increase of 13 % - a difference of 1%.

With such observations that are consistent with the whole myriad of tested amino acids, it is apparent that HumaPro's formulation allows the amino acids to bypass the internal factors that influence interindividual differences in the rate of appearance of amino acids. In addition, there appears to be less competition between amino acids that share the same transporter. For example, the ratio of appearance of the BCAA's (Leucine, Isoleucine, Valine) in whey is 1:1:0.5 while HumaPro's ratio is 1:1:1. With a more balanced ratio, the BCAA's can better induce a physiological response that is more well balanced than that with an unequal ratio. Due to the different amino acid profiles found in whey, BCAA who share a common transporter might compete and therefore displace each other resulting in an unbalanced ratio of BCAAs in plasma. HumaPro's formulation has a fixed ratio of BCAAs that prevents this altered appearance of BCAAs.

## Metamatrix Plasma Amino Acid Results From HumaPro® Ingestion

Null Hypothesis: Supplementation with HumaPro® does not increase plasma amino acids in ratios appropriate to complete human utilization and significant results reflecting superior anabolism.

Alternative Hypothesis: Supplementation with HumaPro® increases plasma amino acids in ratios appropriate to complete human utilization and significant results reflecting superior anabolism.

The data provided from Metamatrix were analyzed via a paired one tail t-test to determine if there existed any significant differences in amino acid levels post HumaPro® supplementation. Each amino acid was matched and analyzed separately to observe statistical significance ( $p < 0.05$ ).

The outcome of the results are as follows:

Lysine	0.000121696	Significant
Methionine	0.130825883	Not Significant
Tryptophan	0.000947124	Significant
IsoLeucine	0.002863116	Significant
Leucine	0.000135854	Significant
Valine	6.20599E-05	Significant
Phenylalanine	0.006736277	Significant
Threonine	0.00834951	Significant
Arginine	0.253500253	Not Significant
Taurine	0.122077228	Not Significant
Serine	0.131103959	Not Significant
Glycine	0.083443871	Not Significant
Histidine	0.090045159	Not Significant
Tyrosine	0.170145598	Not Significant
Glutamic Acid	0.14139723	Not Significant
Arginine	0.253500253	Not Significant
Citrulline	0.328017425	Not Significant
Ornithine	0.405397971	Not Significant
Glutamine	0.359137429	Not Significant
Asparagine	0.227640744	Not Significant
Aspartic Acid	0.259249866	Not Significant
Phenylalanine/Tyrosine	0.054482636	Not Significant
Glutamic acid/Glutamine	0.167278779	Not Significant
Tryptophan/LNAA	0.14038725	Not Significant

This data suggests that the null hypothesis was rejected for Lysine, Tryptophan, IsoLeucine, Leucine, Valine, Phenylalanine, Threonine. As for the remainder of the amino acids tested the null hypothesis was failed to be rejected and thus statistical significance was not concluded. However in all subjects remaining amino acid ratios post HumaPro® ingestion did stabilize to optimal levels without an increase

in negative waste metabolites as validated in the 24hr negative waste urea tests. Therefore plasma amino acid ratios significant to optimal health, performance and recovery from supplemental use of HumaPro has been validated in primary studies.

Tryptophan and phenylalanine are important precursors for the amino acids serotonin, dopamine, norepinephrine, and epinephrine, thus adequate levels of these amino acids should be considered an important aspect regarding the benefits they pose for central nervous system functioning.

Threonine is an important amino acid that the body utilizes to produce ATP via the Krebs cycle. In addition, Threonine enables structural support for muscle tissue by promoting elastin and collagen production.

Leucine, Isoleucine, and valine are the branch chain amino acids that are central for initiating muscle protein synthesis as well as insulin modulation that help in nutrient repartitioning.

The statistical significance of these amino acids should be observed within this physiological context. Further studies will be needed to elucidate these mechanisms.

\* The elevation of any single EAA out of ratio to the other 7 EAAs results in a decrease in NNU due to limitations set. Proper ratios for humans of EAAs (Essential Amino Acids), particle size as well as creating a delivery sequence for optimal utilization are paramount to positive results.

## **Urea Nitrogen Waste 24 hour Urine Collection Test results:**

Urea is a major waste product of protein and amino acid metabolism. Therefore the 24 hour excretion results post 12 hour fasting and subsequent ingestion of protein(s) or amino acids will provide significant validation of NNU (Net Nitrogen Utilization which provides the positive nitrogen balance necessary for recovery and growth) vs. NC (Negative catabolite value or waste from a given protein source). In this study after fasting 6 subjects ingested either 56g of whey isolate or 10 tablets x 4 of HumaPro® then crossed over for a second 12 hour fasting period and ingested the opposing test compound. It should be noted that 10 tablets of HumaPro® has been previously validated in another preliminary clinical to provide the same NNU as 56g of whey isolate protein thus the testing protocol equivocal would be 10 tablets of HumaPro®. Thus the protein metabolic waste urea expressed from 4 times the equivocal dosage in theory should be similar to that of 224g of the whey isolate. The results show a 3 fold increase in the urinary waste product from the 56g of whey isolate subjects ingested as compared to 40 tablets of HumaPro®.

### **Summary:**

The metabolic waste from metabolism of proteins is toxic to human physiology thus reduction or removal results in a greater recovery, repair and growth potential for proteinacious tissues. Increased NNU on the other hand result in a significant increase in anabolism. Combined the anabolic environment is further augmented. Therefore HumaPro® is significantly superior to whey proteins or common EAA products in decreasing systemic toxicity and supporting a positive anabolic environment.



QUEST DIAGNOSTICS INCORPORATED

SPECIMEN INFORMATION  
SPECIMEN: OW364810E  
REQUISITION: 6648505

COLLECTED: 09/15/2010  
RECEIVED: 09/17/2010 23:39 PT  
REPORTED: 09/21/2010 07:36 PT

PATIENT INFORMATION

DOB: [REDACTED]  
GENDER: [REDACTED]

ID: [REDACTED]  
PHONE: [REDACTED]

REPORT STATUS FAX COPY

ORDERING PHYSICIAN  
COHEN, RICHARD A

CLIENT INFORMATION  
N31010297  
BIOLETICS  
RICHARD COHEN, MD

AARRSSS

COMMENTS:

Volume: 1600/24

Test Name	In Range	Out of Range	Reference Range	Lab
UREA NITROGEN, 24 HOUR URINE (W/O CREATININE)				EN
UREA NITROGEN, 24 HR UR	13		6-17 g/24 h	

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PERFORMING LABORATORY INFORMATION

EN QUEST DIAGNOSTICS-WEST HILLS, 8401 FALLBROOK AVENUE, WEST HILLS, CA 91304-3226  
Laboratory Director: LEE H. HILBORNE, MD, CLIA: 05D0642827

LIST OF RESULTS PRINTED IN THE OUT OF RANGE COLUMN:

Reference: Subject-A 56 grams Whey protein isolate



QUEST DIAGNOSTICS INCORPORATED

SPECIMEN INFORMATION  
SPECIMEN: 0W017187E  
REQUISITION: 6648504

COLLECTED: 07/28/2010  
RECEIVED: 07/29/2010 22:57 PT  
REPORTED: 08/02/2010 14:00 PT

PATIENT INFORMATION

DOB: [REDACTED]  
GENDER: F FASTING: U

ID: [REDACTED]  
PHONE: [REDACTED]

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ORDERING PHYSICIAN  
COHEN, RICHARD A

CLIENT INFORMATION

BIOLETICS  
RICHARD COHEN MD

AARRSSS

COMMENTS:

Volume: 3700/24

Test Name	In Range	Out of Range	Reference Range	Lab
UREA NITROGEN, 24 HOUR URINE (W/O CREATININE)				EN
UREA NITROGEN, 24 HR UR		5 L	6-17 g/24 h	

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PERFORMING LABORATORY INFORMATION

EN QUEST DIAGNOSTICS-WEST HILLS, 8401 FALLBROOK AVENUE, WEST HILLS, CA 91304-3226  
Laboratory Director: LEE H. HILBORNE, MD, CLIA: 05D0642827

LIST OF RESULTS PRINTED IN THE OUT OF RANGE COLUMN:

UREA NITROGEN, 24 HR UR	5	L	6-17 g/24 h
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Reference: Subject-A 10 tablets 4 times



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SPECIMEN INFORMATION  
SPECIMEN: OW198728E  
REQUISITION: 6648494

COLLECTED: 08/24/2010 08:30 PT  
RECEIVED: 08/25/2010 22:54 PT  
REPORTED: 08/27/2010 14:00 PT

PATIENT INFORMATION

DOB: [REDACTED]  
GENDER: F FASTING: N

ID: [REDACTED]  
PHONE: [REDACTED]

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ORDERING PHYSICIAN  
COHEN, RICHARD A

CLIENT INFORMATION

BIOLETICS  
RICHARD COHEN MD

AARRSSS

[REDACTED]

COMMENTS:

Volume: 4575/24

Test Name	In Range	Out of Range	Reference Range	Lab
UREA NITROGEN, 24 HOUR URINE (W/O CREATININE)				EN
UREA NITROGEN, 24 HR UR		18 H	6-17 g/24 h	

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PERFORMING LABORATORY INFORMATION

EN QUEST DIAGNOSTICS-WEST HILLS, 8401 FALLBROOK AVENUE, WEST HILLS, CA 91304-3226  
Laboratory Director: LEE H. HILBORNE, MD, CLIA: 05D0642827

LIST OF RESULTS PRINTED IN THE OUT OF RANGE COLUMN:

UREA NITROGEN, 24 HR UR 18 H 6-17 g/24 h

Reference: Subject-B 56 grams Whey protein isolate



QUEST DIAGNOSTICS INCORPORATED

SPECIMEN INFORMATION  
SPECIMEN: OW112369E  
REQUISITION: 6648497

COLLECTED: NOT GIVEN  
RECEIVED: 08/12/2010 23:09 PT  
REPORTED: 08/16/2010 14:00 PT

PATIENT INFORMATION

DOB: [REDACTED]  
GENDER: F FASTING: N  
ID:  
PHONE:

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ORDERING PHYSICIAN  
COHEN, RICHARD A

CLIENT INFORMATION

BIOLETICS  
RICHARD COHEN, MD

ARRSSS

COMMENTS:

Volume: 4300/24

Test Name	In Range	Out of Range	Reference Range	Lab
UREA NITROGEN, 24 HOUR URINE (W/O CREATININE)				EN
UREA NITROGEN, 24 HR UR	7		6-17 g/24 h	

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PERFORMING LABORATORY INFORMATION

EN QUEST DIAGNOSTICS-WEST HILLS, 8401 FALLBROOK AVENUE, WEST HILLS, CA 91304-3226  
Laboratory Director: LEE H. HILBORNE, MD, CLIA: 05D0642827

LIST OF RESULTS PRINTED IN THE OUT OF RANGE COLUMN:

Reference: Subject-B 10 tablets 4 times



QUEST DIAGNOSTICS INCORPORATED

SPECIMEN INFORMATION  
SPECIMEN: OW364811E  
REQUISITION: 6648506

COLLECTED: 09/15/2010 07:00 PT  
RECEIVED: 09/17/2010 23:40 PT  
REPORTED: 09/23/2010 14:04 PT

PATIENT INFORMATION

DOB: [REDACTED]  
GENDER: M FASTING: N

ID: [REDACTED]  
PHONE: [REDACTED]

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ORDERING PHYSICIAN  
COHEN, RICHARD A

CLIENT INFORMATION

BIOLETICS  
RICHARD COHEN MD

AARRSSS

COMMENTS:

Volume: 2200/24

Test Name	In Range	Out of Range	Reference Range	Lab
UREA NITROGEN, 24 HOUR URINE (W/O CREATININE)				EN
UREA NITROGEN, 24 HR UR		26 H	6-17 g/24 h	

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PERFORMING LABORATORY INFORMATION

EN QUEST DIAGNOSTICS-WEST HILLS, 8401 FALLBROOK AVENUE, WEST HILLS, CA 91304-3226  
Laboratory Director: LEE H. HILBORNE, MD, CLIA: 05D0642827

LIST OF RESULTS PRINTED IN THE OUT OF RANGE COLUMN:

UREA NITROGEN, 24 HR UR	26	H	6-17 g/24 h
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Reference: Subject-D 56 grams Whey protein isolate



QUEST DIAGNOSTICS INCORPORATED

SPECIMEN INFORMATION  
SPECIMEN: 0W934096D  
REQUISITION: 6648462

COLLECTED: 07/16/2010  
RECEIVED: 07/18/2010 04:32 PT  
REPORTED: 07/19/2010 14:03 PT

PATIENT INFORMATION

DOB: [REDACTED]  
GENDER: M FASTING: U

ID: [REDACTED]  
PHONE: [REDACTED]

REPORT STATUS FINAL REPRINT

ORDERING PHYSICIAN  
COHEN, RICHARD A

CLIENT INFORMATION

BIOLETICS  
RICHARD COHEN, MD

AARRSSS

COMMENTS:

Volume: 1400/24

Test Name	In Range	Out of Range	Reference Range	Lab
UREA NITROGEN, 24 HOUR URINE (W/O CREATININE)				EN
UREA NITROGEN, 24 HR UR	7		6-17 g/24 h	

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PERFORMING LABORATORY INFORMATION

EN QUEST DIAGNOSTICS-WEST HILLS, 8401 FALLBROOK AVENUE, WEST HILLS, CA 91304-3226  
Laboratory Director: LEE H. HILBORNE, MD, CLIA: 05D0642827

LIST OF RESULTS PRINTED IN THE OUT OF RANGE COLUMN:

Reference: Subject-D 10 tablets 4 times