

dotFIT[™] FirstString[™]

Goal

To provide a product containing ideal performance-enhancing nutrition that can be properly integrated within daily meal planning and training protocols, is also NSF Certified for Sport, and meets NCAA athletic guidelines for carbohydrate/protein content. Based on the current scientific evidence, FirstString (FS) is designed to provide the ideal rapidly digesting powdered "food-form" training formula for size, strength, and performance athletes, further defined as purely anaerobic (e.g., off-season bodybuilders, powerlifters, sprinters, etc.), intermittent (most team sports – i.e., combined intermittent aerobic and anaerobic activity such as football, soccer, basketball, baseball, rugby, hockey) and short to medium distance endurance athletes. Further, the FS food form formula, including the macronutrient ratio (carbohydrate, protein, fat content), is ideal for supporting youth growth and development, including height, pre, and post-puberty. Additionally, because of FS mixing qualities, it serves as a great delivery system for important foods such as fruits, vegetables, milk, etc., often shorted in growing children's diets – i.e., delicious, nutritious smoothies. FS contains a mix of protein (P), carbohydrates (CHO), and fats (F) that, when daily ingestion is timed properly around strenuous activity, FS has the potential to maximize all training-induced results while also helping prepare the body optimally from a nutrition standpoint, for its next training/competitive bout. Used as recommended, FS is strategically formulated so that pre-exercise ingestion helps fill the body's glycogen stores while delivering a rapidly digesting protein containing a high content of essential amino acids (EAA), including the branched-chain amino acids (BCAA), particularly leucine, to reduce muscle breakdown during exercise. Post-exercise ingestion maximizes the muscle protein synthesis (MPS) response during the important so-called exercise-induced metabolic window (0 to ~90 minutes post-activity) when muscle nutrient sensitivity is at its highest point, thus the body's potential for MPS and glycogen replenishment. Therefore, when used as directed within daily meal planning and strenuous activity, FS can maximize the training session, recovery process, and overall gains to help each workout/competition improve upon the last. Additionally, FS is ideal as a weight gain supplement to easily increase food calories for those needing quality weight gain (e.g., muscle).

Rationale

It is well documented that the athletes described above require a specific range of P, F, and CHO based on body weight, activity type, intensity, and duration to maximize performance.^{1,2,3,4,5,6,7,8,9,10} Although a "food form" training supplement should be designed to satisfy these requirements, recommendations are often by-passed based on: 1) body weight or composition goal; 2) preferences; 3) potential for gastric upset; 4) being uninformed, misinformed, or simply choosing to ignore them;^{1,3,11,12,13,14,15,16,17} and 5) experimenting with newly, but undocumented, proposed performance enhancing, or other currently popular diet plans.^{18,19,20,21} Because CHO is the body's preferred energy source and in a constantly higher rate state of flux than protein or fat, it has always been accepted that athletes who are not focused on weight or body fat reduction require a higher percentage of dietary CHO compared to protein or fat if they want to perform at their highest potential.^{1,4,6,7,8,22} Despite tinkering with CHO or fat periodization diets with the goal of delaying fatigue to improve performance (see note below*), CHO intake for most athletes continues to be recommended higher than the other two macronutrients,^{9,10,23,24,25} with the possible exception of shorter completely anaerobic activities such as weight/power training.^{26,27} Therefore, to maximize glycogen (energy) stores for most athletes, especially pre and post-exercise, dietary CHO grams per pound of body weight will exceed protein and fat if improving/maximizing performance is the goal.^{1,7,8,9,10,23,24,25,28,29}

*CHO Periodization Goal: Day-to-day periodization in a meal-by-meal manner (as opposed to chronic periods of CHO restriction or CHO feeding) may maintain metabolic flexibility, allowing completion of high-intensity and prolonged duration workloads on heavy training days, such as interval-type sessions undertaken above lactate threshold. Therefore, train low is for those sessions not so CHO-dependent, such as steady-state-type training sessions performed at intensities below the lactate threshold.^{18,19}



Fat periodization (~50-65% fat and <20% CHO for ~5-6 days [fat adaptation phase], followed by acute restoration of CHO just before and during the endurance event) **Goal:** increase intramuscular triglycerides stores, and enhance the mobilization, transport, uptake, and oxidation of fats. Therefore, a micro-periodization protocol has been proposed to enhance both CHO and fat fuel oxidation to delay fatigue.³⁰

The first nutrition goal for all athletes is to cover protein needs, or MPS cannot optimally proceed, making all exerciseinduced gains fall short of potential, or worse, reverse progress.^{3,9,10,12,31,32,33,34, 35,36,37,38,39} Daily protein requirements to maximize MPS will generally top out at approximately 1 gram per pound of lean body mass (LBM) or body weight.^{2,3,9,10,12,31,32,33,34,35,36,37,38,39} except during extreme dieting,^{3,12,39,40,41} leaving ample room (calorically speaking) for CHO intake to adequately fill the athletes' glycolytic energy system to provide the body the energy potential to perform throughout the given activity at its highest level.^{4,7,8,9,10,18,22,23,24,25} (See carbohydrate recommendation below). Once these two macronutrient needs are met, the remainder of the allotted calories can come from dietary fats.^{1,7,8,9,10,22,23,24,25,42,43} Therefore, depending on the activity and its duration, daily CHO intake for most performance athletes (not engaged in prolonged calorie restriction) generally ranges between 40/50-70% of total caloric intake, protein 15-35% and fats 10-30% (i.e., the remainder). And finally, although supplemental protein by itself before and immediately following activity can decrease muscle protein breakdown and enhance MPS during the so-called "anabolic window." 31,32,36,44,45,46,47,48 supplemental protein with CHO appears to have a greater effect not only on the refilling of glycogen stores but also MPS partially due to an enhanced insulin response.^{9,10,29,46,49,50,51,52,53,54,55} The FS profile of ~2:1 CHO to P ratio and low fat is designed to help fulfill the aforementioned athlete's macronutrient needs throughout the day. Because of its rapid digesting whey protein and specialized CHO mix, FS provides an ideal starting mix or standalone pre/post activity formula to maximize the training/competition session and subsequent outcomes. Mindful that if additional CHO is needed, such as for endurance athletes or CHO loading, it can be added to the mix as needed, including specialized blends. To learn more about special bioengineered carbohydrates, Practitioners can go to the Carbohydrate Structure Database (CSDB, http://csdb.glycoscience.ru)⁵⁶ and the database of Chemical Entities of Biological Interest (ChEBI)⁵⁷ to learn more about advances in applications of the new generation of carbohydrates.

Carbohydrates in Refueling & Rebuilding Muscles

Protein is essential to life, and while carbohydrates are not deemed as such, they are crucial to performance. Therefore, it would be remiss to ignore dietary CHO recommendations for maximizing performance since CHO supplies most of the energy that powers muscular activity. After substantial energy/glycogen depletion, the mean hourly rate of replacement is ~5–6 mmol (or 5–6%), therefore it can take approximately 24 hours to refill stores.^{8,9,10,58} As with MPS, immediately following exercise and up to four hours, ^{36,37,38,39,46} there is a high potential for muscle glycogen storage as a result of the depletion-activated stimulation of the glycogen synthase enzyme and exercise-induced increases in muscle membrane permeability and insulin sensitivity.^{54,55,59} This potential can be reached if CHO is consumed within this period. If not, refueling rates are significantly lower.^{8,9,10,46,51,55} This "window" of opportunity for glycogen storage during the early post-exercise period is part of the "metabolic window" concept (discussed below) because as with muscle protein synthesis rates, glycogen synthesis rates decrease after this time-frame even if CHO feeding is continued properly.^{4,8,9,10,28,46,51} Therefore, although short-term CHO restriction may not hinder an acute performance bout⁶⁰ and notwithstanding the above notes on CHO and fat periodization experimenting, the basic strategy for muscle repair, synthesis and refueling, including maximizing muscle liver and glycogen stores and utilization for performance athletes is as follows:

Carbohydrates Amounts and Timing^{1,4,8,9,10,19,28,46,51,58,61,62}

- Overall CHO intake should be between 40/50-70%, depending on activity type, duration, and intensity, of total calorie intake and spread throughout the day with focus on the pre and post exercise period.
 - Most athletes' CHO range is ~3.6–5.5 g/LB/day to maximize muscle/liver glycogen stores.



- 2-4 hours before exercise (depending on gastrointestinal comfort) consume ~0.5 g/lb of body weight of CHO within the pre-workout meal.
- Begin consuming 0.4-0.5 g/lb of body weight of CHO soon after exercise. Endurance athletes would continue this target each of the next four hours post exercise, before resuming the normal eating pattern. Anaerobic (e.g., off-season bodybuilders, power lifters, sprinters, etc.), intermittent (most team sports i.e., combined intermittent aerobic and anaerobic activity such as football, soccer, basketball, baseball, rugby, hockey) athletes following the immediate post CHO and protein dose, could resume normal eating patterns (e.g., every 3-4 hours) that meet overall energy needs.
 - Basic CHO recommendation ranges based on body weight and activity fuel needs:
 - Low intensity activity: 1.4-2.25 g/lb/day
 - Moderate exercise of approximately 1 hour: 2.25-3.0 g/lb/day
 - Endurance-type program (1-3 hrs/day of moderate-high intensity exercise, such as team sport practices, running, etc.): 2.75-4.5 g/lb/day.
 - Ultra endurance program (>4-5 hrs/day of moderate-high intensity training): 3.6-5.5 g/lb/day
 - Pre-competition ("loading") varies according to duration of exercise:
 - 2.7 g/lb/d <90 min of exercise
 - 4.5–5.5 g/lb/d >90 min of exercise
 - .45–1.8 g/lb final "top-off" 1–4 hours prior to event
 - Try to finish solid foods three hours before the event.
- During exercise (for those interested in more information on types, preferences, or common usages of CHO during training/competition by endurance athletes, see Reinhard et al., <u>"Carbohydrate Intake Practices and Determinants of Food Choices During Training in Recreational, Amateur, and Professional Endurance Athletes: A Survey Analysis</u>⁶³
 - Depending on sport, 3-6 ounces of water or sports drink every 15 minutes.
 - High intensity (> 70% VO₂ Max) exercise >90 minutes, consume 30-60 g of CHO/hour in a 6-8% CHOelectrolyte solution (up to 120 g/hour may be most beneficial in ultra-endurance athletes that can tolerate this amount during activity).⁶⁴
 - Glucose/electrolyte solutions to maintain blood glucose levels, prevent dehydration, and reduce the immunosuppressive effects of intense exercise.
 - Menzies et al., found that ingesting a total of 75 g of CHO/sucrose in small 5 g doses every 5 min enhances running capacity compared with consuming the same amount of CHO in a single bolus after 75 minutes. Further, in the frequent feeding condition during the first 75 minutes, muscle glycogen was spared leading to an increased exercise capacity.⁶⁵

Protein in Refueling & Rebuilding Muscles

For a complete scientific update on protein, and especially whey protein which is in FirstString, including but not limited to: structures, functions, types/sources, mechanisms of action in body fat reduction/dieting, muscle hypertrophy/performance, requirements with rational, timing, anabolic response/threshold (whole body protein synthesis), muscle full effect, aging, immunity, whey protein superiority, safety, etc., the reader is referred to the <u>WheySmooth</u> in the Practitioner Dietary Supplement Reference Guide (PDSRG). Therefore, the below summary content is directly related to the proper protein recommendations for maximizing skeletal muscle hypertrophy and performance.

Protein Amounts and Timing

• Daily protein requirements to maximize MPS/hypertrophy/performance will generally top out at approximately 1 gram of high quality protein (e.g., whey/dairy, fish, poultry, lean beef, etc.,) per pound of lean body mass (LBM) or



body weight daily,^{2,3,9,10,12,31,32,33,34,35,36,37,38,39} (15-35% of total calories) except during extreme dieting when protein needs increase in order to preserve LBM.^{3,12,28,40,41}

o 1 g/lb/day of body weight works for virtually all non-overweight athletes under most conditions.

- The amount of protein per meal in non-calorically restricted athletes, regardless of the ambiguous "muscle full effect," to at a minimum maximize MPS (positive net *muscle protein* balance) should be primarily determined by total muscles worked,^{66, 67,68} body weight or LBM, age (older athletes require more protein than younger counterparts⁶⁹) and therefore, suggested to be 0.18-.25 g/lb of LBM (0.4-.55/g/kg body weight).^{70,71}This number is purely academic ("nice to know") when evenly dividing proper daily protein intake.*
- Protein intake should be evenly distributed throughout the day, generally 3-4 hours apart to coincide with the natural rhythmic MPS and muscle protein breakdown (MPB) cycles (see below).
 - Example:200 lb athlete consuming 200 g/protein/d would consume ~35 g/meal if consuming four traditional meals and a pre and post training protein/CHO supplement both containing ~35 g protein
- Training/competition days consume a fast-acting protein and carbohydrate formula ~30-40 minutes before activity and repeat the same formula immediately following activity to take advantage of exercise-induced heightened nutrient sensitivity (see section below, "Exercise-Induced Metabolic Window").
- Ideal MPS protocol may also include a final dose before bedtime since sleep time is generally the longest lapse in which there would be a reduced extracellular EAA presence, and protein ingestion before sleep has demonstrated increases in MPS rates during overnight recovery from exercise bouts.⁷² In an update on pre-sleep protein supplementation studies, Snijders et al. found protein ingestion prior to sleep can be applied in combination with resistance type exercise training to further augment the gains in muscle mass and strength when compared to no protein supplementation and that 30-40 grams may be most effective due to length of sleep time.⁷³
- Aging athletes: experts now recommend up to 0.8 g/lb of **body weight**, for older adults (exercisers or not). This increase demonstrates greater maintenance of net protein balance and would be sufficiently covered with the same amount (1 g/lb/LBM/d) that works for younger active humans.^{74,75,76,77,78,79,80,81,82}

*Note: although size, age, health, genetics, energy balance and activity will determine a person's protein requirement for maximizing MPS throughout all stages of life, the exact amount per individual or meal is academic, not necessarily practical since the total daily protein is divided throughout the day in generally 3–4-hour intervals to maximize performance/hypertrophy. In other words, each serving will automatically cover the skeletal muscle anabolic requirements to maximize exercise induced hypertrophy or performance regardless of individuality.

Protein (Amino acid) Timing

Muscle protein dynamics (breakdown and synthesis) involve approximately four hour cycles (Figure 4) in which following digestion of a protein rich meal, synthesis is greater than breakdown but returns to baseline within four hours at which time breakdown begins to exceed synthesis until another protein meal is consumed and digested.^{2,31, 83,84,85} Therefore in exercisers/athletes, it has been long proposed that to maximize MPS, a person should consume protein in three to four hour intervals including before and after exercise when there is an exaggerated potential for MPS (see next section and Figure 5). Arguments often surface on the timing of protein ingestion's relationship in maximizing MPS, such as, albeit in the minority, "it doesn't matter when you eat your protein as long as you get enough daily protein."^{36,86} For serious hard training athletes, the argument is unintuitive and frankly meaningless. Considering its well documented (see references above) for athletes to maximize MPS, they are recommended to eat ~1 g/lb/LBM/day of protein (many sports nutrition experts recommend protein at .73-1.0 g/lb of **body weight/**day and higher amounts during body/weight loss), why wouldn't you spread it out throughout the day to match the protein balance cycles including before and after a workout?⁸⁷ Consuming a day's total recommendation of protein in two to three meals daily would be uncomfortable at best, and over time, based on being in a negative protein balance more hours than a positive one, logically the subject should have less exercise induced gains compared to a counterpart consuming protein when the body is ready to use it based on natural cycling – i.e. every three to four hours.^{9,37,38,46,88,89}



Further, there would be no possibility of a MPS advantage, shown in many studies, if not consuming protein (fast acting, such as a shake) before and/or after training.^{9,37,38,46,47, 90,91,92,93,94,95,96,97}

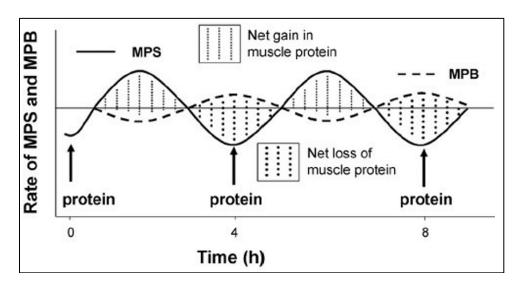


Figure 4 - Natural Muscle Protein Balance in Non-exercising Young Adults. Source: Adapted from Phillips et al.³¹

The processes of MPS and MPB in post-pubertal healthy humans up to ~30 years in the normal (non-exercised) state. Protein synthesis fluctuates with protein intake and fasting across the diurnal cycle, and increases in muscle protein mass are equaled by losses. Note: Cost of MPS & MPB (protein turnover): 1.04 Kcal/g and ~1-2% of all protein replaced daily.^{31,33,34,97}

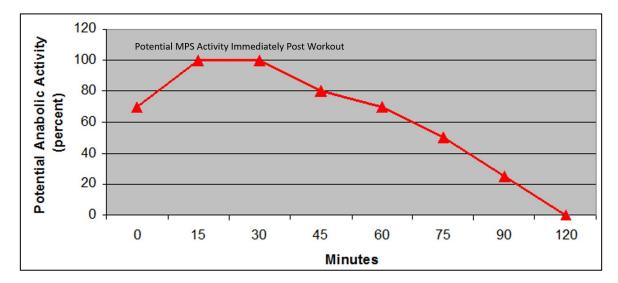
Exercise Induced "Metabolic Window"

The so called "metabolic or anabolic window" is a period when there is an exaggerated anabolic potential created by exercise and realized by the simultaneous presence of exogenous amino acids and CHO within a specific timeframe. This convergence results in a period of enhanced MPS and glycogen restoration that would potentially contribute to improved daily recovery, and thus greater long-term gains, as opposed to no AA or CHO feeding during this opportune timeframe where nutrient sensitivity is heightened from exercise-induced muscular damage and glycogen depletion. As shown in Figure 5, the proposed timeframe would begin immediately following exercise at which point the anabolic potential would be at its highest and slowly wane until ending 90-120 minutes postexercise. Thus the "window" is open widest upon exercise cessation, slowly closing to baseline during the next 90-120 minutes. Although theoretical, there is no downside to this practice. Yet as many studies have demonstrated, there may be a significant recovery/MPS incremental upside that may not be accounted for at another point in time without this regular pre/post exercise feeding (i.e., not a complete "catch up"), even when all things are equal (e.g., total daily protein and CHO intake, exercise protocol, etc.). Logically then, along with better glycogen recovery, thus improved energy status for the next exercise bout, this practice may also have slow accruing benefits to an athlete's competitive lifespan, as well as exercisers over a lifetime of activity, possibly prolonging years of desired movement modalities and independence.⁴⁸

Because exercise sensitizes muscles to a hyper-aminoacidemia environment,⁹⁸ the long-held practice by strength and physique/bodybuilding athletes of ingesting a fast acting protein (with or without fast acting carbohydrates) via liquid delivery system (i.e. powder mixes) before and immediately after exercise is now mainstream and commonly recommended to serious/competitive athletes^{37,38,46,51,88,99} and popularized by the everyday exerciser as a safe and effective means of maximizing and potentially prolonging exercise results.^{47,87,90,92,93,94,95,101,102,100,101,102} There is an exaggerated MPS response if and when exercise, and endogenously supplied AA converge -i.e., the so-called exercise-induced "Anabolic [or metabolic] Window."^{31,32,48,50,51,102,103,104}



Figure 5 - Closing of the Proposed Exercise-Induced "Anabolic Window" (Source: Adapted from Ivy et al.⁵¹)

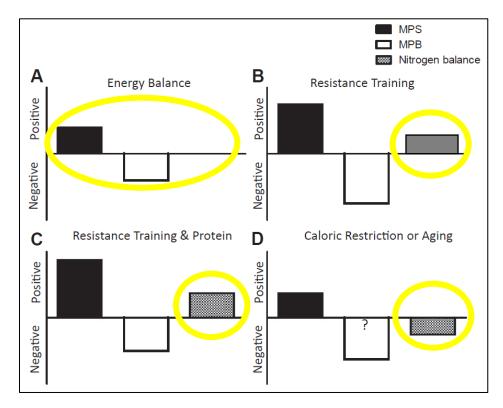


MPS and glycogen synthesis potential (channel activation, nutrient sensitivity, etc.) reach their highest respective points almost immediately post exercise, returning to baseline within 2-3 hours, leading athletes to attempt to capture the peak activity by supplying quick acting protein/EAA to improve MPS outcomes as opposed to no feeding during this timeframe of an exaggerated MPS response when exercise & AA converge -i.e., the so-called "Anabolic Window."

Earlier studies, based on AA MPS mechanisms of actions in the face of exercise described above, suggested that dosing protein pre and post exercise would help establish the EAA concentrations at necessary levels in the affected muscles, to not only deliver their molecular signals to trigger MPS at this opportune time when the body is most responsive, but also to reduce muscle protein breakdown (MPB).^{31,32,104,105} Supplementation of complete fast acting protein before and after exercise has demonstrated an incremental MPS benefit when everything else (diet, exercise and total protein) was equal. ^{44,50,51,106,107} See Figure 6. Subsequent pre- and post-exercise protein or EAA supplementation (with or without carbohydrates) studies have duplicated these earlier results demonstrating improved MPS and recovery compared to no feeding in this "window," hence this practice has become part of the total daily protein ingestion timing protocol recommendation.^{37,38,46,47,51,87,88,90,91,92,93,94,95,99,101,102}



Figure 6 - Incremental Overall Nitrogen Retention (skeletal muscle) with Pre/Post Exercise Feedings Adapted from Devries,¹⁴⁴ Philips,³¹ and Pasiakos³²



A: No net increase (nitrogen balance) in skeletal muscle (SM) as in young healthy (~20-30 yrs.) non-exercising adults, MPS=MPB. B: Addition of exercise and normal diet with adequate protein but without immediate pre/post AA feeding, MPS≥MPB up to point. C: Pre/post AA feedings (anabolic windows) in addition to normal diet and exercise may produce greater daily MPS signaling and activity (including through less MPB), which may be incremental to normal feedings

D: Caloric restriction and/or ageing lead to MPB>MPS, in which increased protein intakes and exercise can minimize or reverse up to a point based on deficit, age and/or training experience

The two major opportunities that present themselves in this exercise induced "anabolic window" are 1) reducing excessive exercise induced muscle damage, and although MPB is necessary to stimulate exercise increases in MPS, too much MPB may be counterproductive since exercise protocols that induce hypertrophy show an eventual decrease in muscle damage, compared to the initial phase of exercise, while hypertrophy becomes measurable and continues to manifest, ¹⁰⁸ (to be sure, androgens/testosterone have anti-catabolic actions via inhibition of the actions of the catabolic hormone, cortisol, that leads to increases in MPS.^{109,110} See Figure 7). Therefore, during intense training, reducing MPB by a slight protein-induced simulation of insulin (insulin may primarily regulate muscle anabolism through its known inhibitory effects on MPB¹¹¹) and presenting EAA to the affected tissues before and during activity,^{32,102,112,113} may more guickly and continuously support enhanced remodeling.^{84,93,102,114,115} Further, Gieske et al. demonstrated that protein before exercise can increase rates of energy expenditure and fat oxidation compared to placebo or fasting before exercise, which may also contribute to the fitness end goals.⁴⁷ 2) MPS (and glycogen synthesis) potential is at its highest point (see Figure 5) immediately post exercise but this sensitivity also wanes quickly, ^{32, 116,117,118} thus there is no harm and may be a benefit (as noted above), to an almost immediate delivery of a fast releasing protein/EAAs (carbohydrate as necessary¹¹⁹) to potentially maximize the activated MPS machinery by creating a hyper aminoacidemia environment.^{44,50,51,102,107,117,120} Again, you have to consume a known amount of daily protein split throughout the day anyway, so it might as well include a pre and post exercise portion.¹²¹



Post exercise ingestion would take place independently of whole foods in order to minimize normal EAA clearance by the splanchnic bed and perhaps more importantly, to avoid slower gastric emptying by accompanying foods since the goal is rapid hyper-aminoacidemia during this timeframe.^{90,102, 122,123} Timed ingestion of whey protein both pre- and post-workout^{114, 124,125,126,127} facilitates a more rapid absorption of amino acids into the bloodstream and their subsequent delivery to the target tissues with less splanchnic extraction, when compared to other sources of proteins.^{90,91,92,93,94,95,96,106, 128,129,130,131,132,133,134,135,136,137,138,139,140}

Summary

Like most nutrition recommendations, protein requirements are individual including being partially related to preference, and researchers are still in discovery of protein's anabolic threshold per meal (3 to 4-hour intervals), based on defining the anabolic response as whole-body protein turnover or net protein balance. MPB is unequivocally part of the MPS process for all humans, and whether using nutritional interventions (high protein or EAA intake) to reduce MPB from exercise induced damage to yield a better MPS/recovery response, remains unknown but appears likely and may be important to the competitive lifespan of athletes. Nevertheless, in the properly fed athlete, meeting daily protein requirements (1 g/lb/LBM or body weight) divided between four to six meals will cover any differences in scientific opinions. Moreover, no matter the final destinations, almost all protein/AAs consumed will be utilized somewhere with higher than recommended amounts for supporting MPS deemed safe. Lastly, going beyond protein's anabolic contribution may have other personalized benefits such as satiety and lifetime weight control, and the only downside would be if the excess protein not used for MPS was taking the place of needed CHO to properly fuel activities and support the proper anabolic hormonal environment.

In summary, the current scientific consensus is as follows: the amount of protein per feeding (~3-to-4-hour intervals) that maximizes recovery including the desired exercise-induced musculoskeletal/cardiovascular adaptations (e.g., hypertrophy, BMD, muscular endurance, etc.) is proposed to be **0.18 to .25 g/lb of body weight (0.4 to .55 g/kg body weight).**

Protein Safety and Upper Limit

Throughout each section of this document, protein intake safety and efficacy are discussed and referenced at or above the new proposed recommendations (1-1.2 g/lb/LBM/day) for each circumstance including age groups, with no known adverse effects. Additionally there is no established Tolerable Upper Limit (UL) for protein and a wide range of daily intake is now within the DGAs.^{141,142} The Institute of Medicine's (IOM) review of studies examining adverse effects of high-protein diets was unable to identify a level of daily protein that increased the risk of health problems including renal, osteoporosis, kidney stones, obesity, etc.¹⁴² One common question has always been the amount of protein that negatively effects renal function. Currently, there is no evidence that increased urea formation or changes in glomerular filtration rate from protein intake beyond nitrogen balance or within DGA guidelines (10-35% of total calorie intake) causes kidney damage in healthy persons.^{143,144,145} In fact, clearance becomes more efficient with higher protein intakes.^{146,147} Bone health was another common concern with high protein intakes. A systematic review by Darling et al. on the subject determined there was insufficient evidence that high protein intakes effect bone health either positively or negatively,¹⁴⁸ and recently possibly positive,¹⁴⁹ and especially with adequate dietary calcium.^{150,151} The Groenendijk et al. systematic review supports that a protein intake above the current RDA may reduce hip fracture risk and may play a beneficial role in bone mineral density (BMD) maintenance and loss in older adults. ^{152, 153} The bottom line is that chronic protein intake two to four times the RDA and up to 35% of daily energy intake has been shown to be safe and effective for healthy individuals as long as protein is not replacing other necessary nutritious foods. 38,46,141,142,144,146,147, 154,155,156,157,158,159,160

Carbohydrates with Protein to Maximize Performance and Hypertrophy

As described above, daily CHO intake generally should be higher than protein intake to adequately fill the athlete's glycolytic energy system to provide the body the energy potential to perform throughout the given activity at its



highest level.^{1,4,7,8,9,10,18,22,23,24,25,28,29} Additionally, although supplemental protein by itself before and immediately following activity can decrease muscle protein breakdown and enhance MPS during the so-called "anabolic/metabolic window,"^{31,32,36,44,45,46,47,48} supplemental protein with CHO appears to have a greater effect not only on the refilling of glycogen stores, but also MPS partially due to an enhanced insulin response.^{9,10,29,46,49,50,51,52,53,54,55,161,162,163,164,165,166,167}

Insulin, Leucine and MPS

Insulin is a powerful anabolic hormone¹⁶⁸ that reduces muscle breakdown and allows the essential amino acid leucine to effectively function as the major trigger of MPS.^{50,112,137,153,168,169,170} Of all the AA necessary for protein synthesis, leucine is considered the most important, and in fact has been indicated as the sole "initiating" stimulator of MPS, thus a potential limiting factor in MPS.^{50,117,170,171,172,173,174,175,176} Leucine interacts with two mTOR regulatory proteins: mTOR raptor and Ras homolog in the brain (or Rheb).^{177,178} The proposed amount of leucine per dose to maximize MPS has been estimated to be between 2.5-4.0 grams (depending on size, age and activity) and referred to as the leucine threshold.^{31,106,175,179,180}

Carbohydrates' Effect on Catabolic and Anabolic Hormones

Leucine cannot regulate protein synthesis effectively without the presence of insulin.^{50,169,181} Most importantly for hypertrophy and performance goals, high (or recommended levels) versus low CHO intake also favorably alters the overall hormonal environment to help maximize the anabolic net response, especially hypertrophy.^{182,183,184} The <u>Whittaker et al. review</u> titled, *Low-carbohydrate diets and men's cortisol and testosterone: Systematic review and meta-analysis*, concluded "Resting and post-exercise cortisol increase during the first three weeks of a low-carbohydrate diet. Afterwards, resting cortisol appears to return to baseline, while post-exercise cortisol remains elevated. High-protein diets (low CHO) cause a large decrease in resting total testosterone (~5.23 nmol/L)."¹⁸⁵ This hormonal alteration from chronic low CHO intake within a high protein diet, would be unfavorable to muscle hypertrophy and long-term performance outcomes since cortisol (see **Figure 7**) is catabolic and testosterone is anabolic.¹⁰⁹

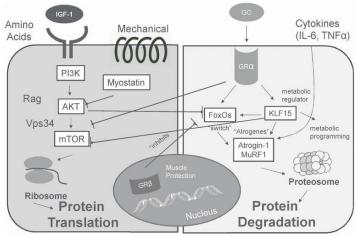


Figure 7 - In skeletal muscle glucocorticoids (e.g., cortisol) produce a catabolic effect that is opposite that of insulin/IGF-I via GRα.¹⁰⁹

The catabolic actions of cortisol result in muscle proteolysis (breakdown) occur mainly through the ubiquitin–proteasome and lysosomal systems.¹⁸⁶ These proteolytic systems, increase the expression of genes involved in atrophy ("atrogenes"*), which in turn target proteins for degradation by the proteasome machinery.¹⁸⁷ Cortisol may also blunt skeletal muscle protein synthesis by inhibiting IGF-I signaling (anabolic muscle growth factor), and increasing myostatin signaling, a muscle catabolic growth factor, contributing to muscle atrophy^{186187,188}

*Atrogenes include transcription factor FOXO, a major switch for the stimulation of several atrogenes, and two ubiquitin ligases atrogin-1 and MuRF-1, involved in the targeting of protein to be degraded by the proteasome machinery, and LC3^{186,187,189}



Studies Using Co-ingestion:

- Cockburn et al. demonstrated that consuming milk-based CHO and protein after muscle-damaging exercise is beneficial in attenuating decreases in muscle performance and increases in active delayed onset muscle soreness (DOMS). ¹⁹⁰
- Betts et al. reviewed the potential benefits of protein co-ingested with carbohydrate in prolonged exercise recovery and suggested that when CHO intake is low, the inclusion of protein may at least partially compensate for the limited availability of ingested carbohydrate. Additionally, it may increase the drive to exercise; blunt exercise-induced muscle damage; favorably alter metabolism during exercise, or a combination of any of these mechanisms.¹⁹¹
- Saunders et al. found that plasma creatine kinase (CK) levels and muscle-soreness ratings increased significantly
 after the CHO compared to CHO and protein consumption. They also found that late-exercise time-trial
 performance was enhanced with CHO and protein ingestion compared with a beverage containing only CHO
 provided at maximal exogenous oxidation rates during exercise.¹⁹² Although Cathcart et al. found no help with
 DOMS they did find that CHO and protein supplementation compared to CHO alone appears to prevent body mass
 loss, enhance thermoregulatory capacity, and improve competitive exercise performance.¹⁹³
- Costa et al. found that ingestion of CHO and protein immediately after (but not 1 hour after) prolonged strenuous exercise prevented the decrease in neutrophil degranulation but did not alter circulating stress hormone, leukocyte trafficking, or S-IgA responses, thus suggesting positive effects on immune function.¹⁹⁴ The latter was validated more recently by Nieman et al.¹⁹⁵
- Blacker et al. found the consumption of whey protein and carbohydrate supplements alone each resulted in faster recovery of the isometric force of the knee extensors compared to a placebo.¹⁹⁶
- Highton et al. compared the effects of carbohydrate and carbohydrate-protein ingestion on self-regulated simulated multiple-sprint sport performance using the Shuttle Test involving 4 x 15 min blocks of regulated exercise followed by 2 x 15 min blocks of self-regulated exercise. Average running speed declined in the final 15 minutes of the CHO trial only, with protein providing a likely small improvement. The authors concluded "carbohydrate-protein ingestion is likely to enhance multiple-sprint sport exercise performance above carbohydrate, potentially through altered central fatigue or increased protein oxidation."¹⁹⁷
- As expected, Hiroyasu Mori et al. found that the post-exercise accumulation of muscle protein in trained
 resistance exercisers was low compared with that of the untrained men. But interestingly, when protein and
 carbohydrate were consumed immediately after resistance exercise, the effect of protein intake on muscle protein
 accumulation was high in the trained men but showed no effect in the untrained men (compared to 6 hours after)
 suggesting that the "metabolic/anabolic window" is more important to trained exercisers.¹⁹⁸
- McLellan et al. in a systematic review on the use of CHO and protein supplements during and after endurance exercise found that when carbohydrate is delivered at optimal rates during or after activity, protein supplements appear to have no added endurance performance enhancing effect.¹⁹⁹
- In a review by Cermak et al.,²⁰⁰ they confirm that the availability of CHO during prolonged (>2 hours) moderate to high intensity exercise can significantly improve endurance performance. These athletes are advised to ingest CHO at a rate of 60 g/hr (well trained individuals can metabolize up to 90 g/hr) provided the CHO is in multiple fast oxidizing forms. To support rapid post exercise glycogen repletion during the acute recovery phase from exhaustive exercise, athletes are recommended to ingest 0.5-0.6 g/lb/hr of CHO. Interestingly, they found that CHO ingestion during shorter, (45-60 min, including intermittent/team sports), more intense (>75% peak oxygen uptake) training bouts also improved performance although endogenous stores were not the limiting factor. Therefore, the mechanism is proposed to reside in the central nervous system.^{7,200} For athletes with a lower gastrointestinal threshold for CHO ingestion and/or to support muscle protein synthesis immediate post exercise, it is recommended to use less CHO (.35 g/lb/hr of CHO) with protein (0.1-0.2 g/lb/hr) or approximately 2:1 CHO:P.^{7,200}



• In support of CHO and P co-ingestion post exercise to enhance the anabolic environment, Betts et al. showed that following 90 minutes of treadmill running, CHO and whey protein (~2:1) raised growth hormone levels and lowered cortisol compared to equal energy of CHO alone.²⁰¹ Further, co-ingestion of amino acid and CHO is regularly shown to be better than CHO alone in supporting post exercise MPS.²⁰²

Beyond protein's role in repairing exercise induced skeletal muscle damage, the co-ingestion of protein with CHO may further accelerate muscle glycogen content compared to CHO alone, especially under conditions when the CHO-protein solution delivers more calories than a CHO-only solution and/or when CHO intake is suboptimal during short-term recovery from prolonged exhaustive exercise.^{203, 204} Further, at this time there is no consensus of evidence to support protein or CHO ingested separately, or solely for the purpose of maximizing performance or hypertrophy for most competitive athletes, especially endurance competitors. In other words, most athletes who are not overly concerned with low bodyfat will benefit from co-ingestion of CHO and protein (or amino acids) at most feeding opportunities, especially pre and post training/acivity.^{1,4,8,9,10,19,28,46,51,58,61,62,63,64,65190,191,192,193,194,195,196,197,198,199,200,201,202}

Data Summary

From all the above data it appears that a 2.0-4:1 ratio of CHO:P may be an appropriate average daily intake for most performance athletes to maximize training energy and recovery/adaptations, including MPS and glycogen replenishment with power/strength/hypertrophy athletes operating at the lower ratio (~2-2.5:1) and ultra-endurance in the higher ranges (i.e., the longer activity duration, the greater CHO). Additionally, this activity specific individualized ratio would be appropriate for the athletes pre and post activity fast acting formula that is generally recommended to maximize training energy and to take advantage of the so-called metabolic window in recovery/adaptations with the protein content being ~ 0.18 to .25 g/lb of body weight (0.4 to .55 g/kg body weight). Once the protein and CHO needs are established, the remainder of allotted calories can come from dietary fats including omega-3 fatty acids. When athletic performance is the primary goal, the range of macronutrient intake should be as follows: 40-70% CHO, 20-30% protein, 15-30% fat, with protein never being below 1 g/lb/LBM/d for any athlete with ratios adjusted as needed. The advantage of powdered mixes for supplemental purposes is that they can be altered as needed based on personalized CHO, protein and calorie needs along with desired fat content by adding components (e.g., milks, fruits, juices, powdered CHO and mixtures, omega-3 fats, etc.,). Further, many athletes will also add ergogenic supplements such as creatine, beta-alanine, beet juice, etc., to their mixes. The FirstString native formula is an ideal starting mix for performance/size athletes* to alter, or not, as necessary.

*Weight and bodyfat conscious athletes (e.g., physique competitors, fighters in weight classes, etc.,) would use a starting mix with lower calories/CHO to protein such as <u>WheySmooth</u> or <u>AminoFormula</u>, but should be reminded to raise their calories/CHO in the off-season to support energy needs and hormone levels to maximize performance/size gains.

Protein in FirstString

For complete peer review referenced data on whey protein in human health, performance and body composition, the practitioner is referred to the <u>WheySmooth section (pages 1-22) in the Practitioner Dietary Supplement Reference</u> <u>Guide (PDSRG)</u>. Below are the important facts.

The protein in FirstString is predominately whey concentrate and the same that is used in WheySmooth, which is an ion-exchange instantized protein blend containing 90% whey concentrate, 5% whey isolate (cold filtered) and 5% casein for immediate and extended release and easy mixing. Compared to other proteins, whey protein has been shown to be superior in maximizing MPS, health and weight control outcomes based on its unique functional properties including: 1) higher essential amino acid (EAA) content per gram of protein (12.4 g/25 g); 2) higher BCAA (5.6 g/25 g); 3) higher leucine (3 g/25 g); 4) faster digestion to timely amplify MPS during metabolic windows; 5) less splanchnic amino acid (AA) extraction so more AA are directly available for MPS; 6) properly filtered (ultra-filtration) whey concentrate, along with the AAs, retains the desired additional unique growth and health/immune factors/globulins, while eliminating the unwanted lactose.*



In summary, the constituents of whey protein including its comparatively higher leucine and other essential amino acid amounts per gram of protein along with the natural health contributing bio-actives contained in the concentrate, make whey protein sources reign premier in supporting MPS and body composition goals. Further, the digestibility, absorption, and amino acid retention (muscle deposition) score compared to other popular protein sources, validates whey's benefits and therefore, when protein supplementation is included to meet individual recommendations in maximizing exercise/performance outcomes or daily life recovery, whey protein is a first choice when diet restrictions do not impede the selection.

*There is 1.4 g of lactose per serving and therefore unless individuals have been diagnosed with "severe lactose intolerance," which is extremely rare, this amount should have no adverse reaction. As a reference, most lactose maldigesters (majority of people who consider themselves lactose intolerant) can consume 6-12 grams of lactose without major symptoms. As a reference, one cup of milk or yogurt has 12 and 9 g of lactose, respectively.

Carbohydrate – Maltodextrins

FirstString (FS) is primarily designed to be a fast acting ~2.2:1 CHO to protein supplement that can be altered as needed. The carbohydrate content in FS is strategically designed for 1) proper calorie to protein ratio but also allows for adjustments (added foods/fluids into mix) as desired; 2) rapid gastric emptying thus oxidation during pre/post workout periods help maximize MPS and glycogen replenishment within the "metabolic windows"; 3) flavor and easy mixing properties.

Maltodextrin

Maltodextrin is a polysaccharide. It is a lightly hydrolyzed starch used as an ingredient in many food products as a thickener and carbohydrate source.²⁰⁵ Maltodextrin is easily digestible, being absorbed as rapidly as glucose but moderately sweet or sometimes bland making it desirable in food manufacturing.²⁰⁵ Carbohydrates (CHO) in sports are generally placed in two categories - CHO that can be oxidized (used for energy) rapidly (up to ~60 g/hr) and those which are oxidized slower (up to ~40 g/hr).⁴ Maltodextrins like glucose, maltose and sucrose fall in the rapid category.^{4,206} These carbohydrates are digested and absorbed at fast rates making them readily available to working muscle and also allow rapid amino acid absorption from co-ingested protein. These qualities, including maltodextrins' food mixture compatibility, make maltodextrins ideal in a product like FS which is designed to deliver both timely protein and CHO to working muscles and help satisfy a proper daily CHO to protein ratio for performance athletes.^{1,4,8,9,10,19,28,46,51,58,61,62,205,206,207}

Dietary Fat Blend

The dietary fats in FS which are made up of high oleic sunflower oil,²⁰⁸ medium chain triglyceride,²⁰⁹ and safflower oil²¹⁰ supply 11% of total calories to allow 1) rapid digestion of combined protein and CHO as too much dietary fat slows digestion, and ^{211,212} 2) enhanced flavoring and mixing qualities of the product.

Co-factors Including Sweeteners

Co-factors in a protein/CHO powder are combined to deliver better taste with low/no calories, texture, mixing ability, uniform nutrient distribution, ingredient flow and stability, including during cooking or baking, and a practical product shelf life.

Sweeteners Background

Health outcomes or adverse reactions to natural and/or added caloric sweeteners (CS), such as refined sugars, honey, syrups, fruit sugars, sucrose and their constituent molecules, include, but are not limited to obesity, blood sugar spikes, tooth decay and allergic reactions from the residues from their sources of origin, has spawned the need and growing use of non-nutritive sweeteners (NNS).^{213,214,215,216,217,218,219} Further, these issues related to CS have led to prevention policies such as sugar-sweetened beverage taxes and front-of-package labels, may also be incentivizing companies to utilize NNS as a way of reducing CS.^{220,221,222,223} (New FDA label format can be viewed <u>here</u>.)



Recognizing there are industry and cult-like biases towards the use of NNS (none have been validated or accepted),^{224,225,226,227,228} the major scientific bodies around the world have firmly established their safety including for use with children,^{229,230,231,232,233,234,235} thus require no label warnings as added CS and other natural ingredients (e.g. peanuts, shell fish, wheat, dairy, etc.).^{218,220,221,222}

In summary, FDA approved NNS advantages over CS include:

- Higher nutrition per calorie/sweetness to support desired body composition, especially when used to replace CS^{236,237}
 - Sucralose tested best of NNS and sucrose in weight management²³⁷
 - Supports blood sugar (approved for diabetics)^{225,230,236}
- Lower risk of adverse reactions common with "natural" sweeteners (honey, stevia, lactose, fruit sugar residues, etc.)^{217,218}
- Supports weight control versus being a contributing factor in weight gain^{231,236,238,239,240,241,242}
- Approved for children^{231,232,233}

•

Finally, the Martyn et al. review titled "Low-/No-Calorie Sweeteners: A Review of Global Intakes" concluded that "Overall, the studies conducted since 2008 raised no concerns with respect to exceedance of individual sweetener acceptable daily intake (ADIs) among the general population globally. Additionally, the data identified do not suggest a shift in exposure over time, with several studies indicating a reduction in intake."²⁴³

Sweeteners in FirstString

Sweeteners used in FirstString appear at the end of the ingredient list as they are in minute amounts per serving and inert in human metabolism thus no effects within the body other than taste.²⁴⁴ For frequently asked questions (FAQs) on non-nutritive sweeteners click <u>here</u>. Non-nutritive sweeteners (NNS) are those that sweeten with minimal or no carbohydrate or energy. NNS are regulated by the Food and Drug Administration (FDA) as food additives.²²⁹ The FDA approval process includes determination of probable intake, cumulative effect from all uses and toxicology studies.^{229,230} Eight NNS (aspartame, acesulfame potassium, luo han guo [monk] fruit extract, neotame, saccharin, stevia, sucralose and advantame (aspartame analog by Ajinomoto) are approved for use in the United States (click <u>here</u> for a list, uses and metabolism) with acesulfame K and sucralose being among the most popular,²¹⁶ largely because of their unique functional properties in enhancing food products including taste.²¹⁶ As with any fitness supporting food product, the better the taste and versatility, the greater chance of sustained use to support health and fitness goals.

Acesulfame Potassium (Ace-K)

Acesulfame potassium (chemical formula C4H4KNO4S; CAS registry number 55589-62-3) is approximately 200 times sweeter than sugar and is often combined with other sweeteners as an additional flavor enhancer in foods because it is heat stable during baking and environmentally friendly.^{245,246} Ace-K is typically used in frozen desserts, candies, beverages, and baked goods. More than 90 studies support its safety and is used in FirstString to support baking capacity and sweetness.²⁴⁷ For a complete current review on Ace-K, readers are referred to Belton et al.'s "A Review of the Environmental Fate and Effects of Acesulfame-Potassium."²⁴⁶

Sucralose

Sucralose is also a NNS, and is made from sucrose by a process that substitutes three chloride atoms for three hydroxyl groups on the sucrose molecule.^{248,249} Sucralose, a very versatile NNS that is 450–650 times sweeter than sucrose, possesses a pleasant sweet taste and a quality and time intensity profile that is close to that of sucrose, making it a popular NNS.^{216,250} Sucralose has been extensively studied with more than 110 safety studies reviewed by the FDA in approving the use of sucralose as a general purpose sweetener for food.^{229,230,248,251} A primary advantage of



sucralose for consumers is its exceptional stability. It retains its sweetness over a wide range of temperature and storage conditions and in solutions over time. This stability allows manufacturers to create greater tasting foods and beverages and maintain the fresh flavor. Like Ace-K, sucralose is heat stable, meaning that it stays sweet even when used at high temperatures during baking, making it a common sugar substitute in baked goods.^{250,252}

The FDA established an acceptable daily intake (ADI) for sucralose of 5 milligrams per kilogram (Europe's is 7 mg/kg and Canada's is 11 mg/kg) of body weight (mg/kg) per day.*²²⁹ The amount of sucralose per serving in FirstString is ~34 mg.

*Out of safety precautions to protect all sub-groups of people, **the ADI represents an amount 100 times less than the quantity of sucralose found to be safe in research studies**.²²⁹ For a person weighing 150 pounds (68 kg), the US ADI equates to 340 mg of sucralose—the amount found in nine cans of diet soda or more than 28 individual packets of sucralose—consumed, on average, every day over a lifetime. Therefore, you could multiply these numbers by 100 before you would cross a known safety threshold in consumption.

Carboxymethyl Cellulose

Carboxymethyl cellulose (CMC) or cellulose gum is a popular non-toxic cellulose (fiber) derivative, an FDA approved food additive and on the generally recognized as safe list (GRAS).²⁵³ CMC is used in food as a viscosity modifier or thickener, and to stabilize emulsions (emulsifier) in food products.^{254,255} CMC is used extensively in gluten-free and reduced fat food products such as FirstString and other dotFIT powders.²⁵⁶ Use of <u>CMC</u> also ensures smooth dispersion in flavor oils, and improves texture and overall quality.^{255,256}

Xanthan Gum (XG)

Xanthan gum is a water soluble, high molecular weight natural polysaccharide produced by a fermentation process.²⁵⁷ Due to its high molecular weight (2.0 × 10⁶–2.0 × 10⁷ Da) and unique chemistry, xanthan gum shows excellent pseudoplasticity, thickening, and rheological properties, and is highly stable to heat, acid, and alkali making it ubiquitous in food products.^{258,259,260} Because of its safety profile, the United States FDA approved xanthan gum as a food additive in 1969, and European countries followed suit where it is primarily used as a molding agent, stabilizer, viscosifier, and thickener.^{261,262, 263} Additionally, small amounts of XG can enhance taste and prevent insoluble ingredients in juice-type beverages from precipitating. Due to its soft texture and ability to function as a stabilizer it is used for many different formulations with applications in pharmaceuticals, dietary supplements, and food products such as FirstString.²⁶⁴

FirstString & NSF Certification for Sport

NSF Certified for Sport

Although all dotFIT (dF) products are formulated and manufactured with the same rigor, FirstString along with a select group of other dF products undergo an additional test and 3rd party certification for another type of assurance. See <u>http://www.dotfit.com/NSF_Certified_for_Sport</u> for the complete line of dotFIT NSF Certified for Sport (NSFCS) products. In addition to the dF standard of evidence-based programming, formulas, and 3rd party testing, the addition of the NSFCS process ensures collegiate and professional athletes that they are protected from unwarranted suspensions due to banned substances in supplements. Therefore, not only are the contents tested to match the label, but the program also includes a test for banned substances that can creep into products during the manufacturing process because of unprotected, non-segregated mixing rooms or worse, deliberate spiking of illegal ingredients. Collegiate, professional, other drug-tested athletes and their team management require this assurance to protect themselves from tainted products commonly found in commercially available dietary supplements in mass-market outlets.^{265,266,267,268,269}



About NSF

To meet the growing demands of athletes, coaches and all those concerned about safety and banned substances in sports supplements, NSF International created the <u>NSF Certified for Sport® Program</u>. The program's objective is to certify that participating sports supplement manufacturers have met NSF's stringent independent certification process guidelines, which were developed through a consensus process involving regulatory, sports industry and consumer groups. This program, which focuses primarily on the sports supplement manufacturing and sourcing process, provides key preventive measures to:

- Protect against the adulteration of products.
- Verify label claims against product contents.
- Identify athletic banned substances in the finished product or ingredients.

NSF developed and maintains the only accredited American National Standard to certify dietary supplements, NSF/ANSI Standard 173. NSF's history of independence led to a partnership with the National Football League (NFL) and the NFL Players Association (NFLPA) to develop and administer the NFL/NFLPA Supplement Certification Program, specifically for professional football but used across all sports.

The NSF Prohibited Substances List includes banned substances, identified by leading sports organizations, such as the World Anti-Doping Agency (WADA), the NFL and Major League Baseball (MLB). The NSF Certified for Sport[™] Program certifies products and inspects facilities for a range of substances. Click here for more on <u>NSF Certification program</u> and products, such as dotFIT.

FirstString Summary

FirstString is NSF Certified for Sport and complies with the NCAA Bylaw 16.5.2.g related to the carbohydrate/ protein content of a supplement. FirstString's (FS) macronutrient profile of approximately 60% CHO, 30% protein and 10% fat is in accordance with current scientific evidence and recommendations that supports maximizing muscle protein synthesis (MPS) and performance for the majority of athletes and especially those with the primary goal of increasing size, strength, and speed. This formula has particular relevance for athletes of all ages involved in "intermittent sports" (e.g., team sports) where the actions are generally intermittent high-intensity movements while executing sport-specific skills over a prolonged period of 1-3 hours (e.g., football, basketball, soccer, rugby, hockey, lacrosse, baseball, etc.). Performance during intermittent sports is dependent upon a combination of anaerobic and aerobic energy systems that are powered primarily by CHO, thus requiring a continuous intake of between 40/50-70% of total caloric intake (TCI). FirstString's macronutrient profile is also ideal for the primarily anaerobic athlete, who is not restricting caloric intake, such as off-season bodybuilders, power lifters, sprinters, etc. and most mid-range endurance athletes. During prolonged dieting for aggressive weight and body fat goals, athletes would switch to WheySmooth and/or AminoFormula. Long or ultra-endurance athletes who require higher CHO intake can add CHO to the FS mix as needed (e.g., CHO powders of choice, fruits, juices, etc.) or simply maintain daily desired macronutrient profile with daily foods when incorporating FS.

Whey proteins have proven to be superior to other protein sources in stimulating MPS and therefore FS uses an ionexchange instantized protein blend containing 90% whey concentrate, 5% whey isolate (cold filtered) and 5% casein for immediate and extended release and easy mixing along with co-factors that give the product its desirable taste, texture, and stability. The CHO source is predominately maltodextrins for fast acting fueling and refueling of muscles. The combination of FS fast acting CHO and protein sources make it ideal to timely amplify MPS during the so-called metabolic/anabolic window. Finally, because of the macronutrient profile, FS is also designed to supplement the overall diet in a manner that can maximize long-term muscle gains by giving the user the ability to timely add protein and CHO in percentages that have been shown to be the most conducive in supporting a continuous anabolic environment.



Typical Use

FirstString is for athletes of all ages including those who are drug tested and whose primary goals are maximizing growth, development and performance including MPS and recovery from strenuous activity.

- As a pre-workout supplement, consume the amount below 30-40 minutes prior to activity based on athletic body size:
 - 100-150 lbs 1.5 scoops
 - 151-220 lbs 2 scoops
 - o 221-300 lbs 3 scoops
 - Greater than 300 lbs (e.g., adult American football linemen, World's Strongest men, etc.,) 4 scoops
- Immediately following training, repeat the same dose unless also using AminoFormula (see <u>muscle stacking</u>) at which time you would consume FS ~30 minutes following the immediate AminoFormula post exercise dose.
- As a meal replacement or weight gain supplement, use as needed throughout the day to meet individual goals for protein, CHO, calorie, and nutrient timing.
- Anyone wanting a great tasting, convenient meal replacement and/or additional protein source.
- Individuals with compromised appetite to shore up nutrition needs, especially in older frail populations.
- Youth athletes to maximize growth and development (including height) and serve as a delivery system for important nutrition often missed by youngsters (e.g., fruits, vegetables, milk, etc.,) i.e., daily smoothies.

Safety

FirstString is considered a food product, so adverse events, precautions, or contraindications with any ingredients in FS are rare or unknown in the general population when supplementing the diet properly, as described above. The section below is a high-level summary related to specific subpopulations. Qualified practitioners needing more information related to these categories, including drug interactions, are referred to the <u>TRC Natural Medicine Data Base</u> (<u>TRCNMD</u>), which is continually updated with emerging evidence-based data.²⁷⁰

Precautions

Also refer to the Protein, Safety and Upper Limit section above

None known other than people with kidney or liver disease would consult with their doctor when adding any protein or amino acids to their diets.²⁷¹

Note: older data suggested an increase in calcium loss with high protein intakes, which may predispose the individual to an increased risk of osteoporosis.²⁷²However, more recent studies have found the link between protein intake and bone health to be positive^{149,152,153,273,274} (especially when adequate calcium is consumed^{150,151,275}) or no effect.^{148,276} The Institute of Medicine's and other related studies have concluded that levels of dietary protein are not associated with a decrease in renal function with age.^{142,143,144,145,277,278,279,280,281,282}

Contraindications

There is negligible lactose in FirstString (removed during production), therefore it would only be contraindicated in people unable to consume dairy proteins based on a protein structure allergy.^{283,284} Do not simultaneously use the drug LEVODOPA. Theoretically, whey protein might decrease levodopa absorption.²⁸⁵

Adverse Reactions

There should be no adverse effects in healthy users at the recommended doses unless allergic to dairy proteins. Consuming large quantities may cause general gastrointestinal distress, such as bloating, diarrhea, reflux, etc., in susceptible people. Most adverse effects are dose related and rare.²⁸⁶



Upper Limit/Toxicity

Currently there is no upper limit established for protein.^{142,279} Further, chronic protein intake two to four times the RDA and up to 35% of daily energy intake has been shown to be safe and effective for healthy individuals as long as protein is not replacing other necessary nutritious foods.^{33,46,141,142,144,146,147,154,155,156,157,158,159,160}

Summary

Purpose

- Athletes or exercisers with primary goals of maximizing training induced muscle protein synthesis (MPS), replenishment of energy stores, recovery, acute and long-term performance, and body composition goals.
 - Fast acting whey protein and maltodextrins are used to timely amplify MPS during metabolic/anabolic windows before and after exercise and throughout the day, as necessary.
- The base product's carbohydrate (CHO) to protein ratio (~2:1) supports the maximum anabolic response making it ideal as a weight/muscle gain supplement.
 - Two scoops provide 21 grams of whey protein, 45 grams of CHO, 200 mg of calcium, making up 290 quality calories.
 - Ability to deliver the surplus of energy and the nutrients required to be incorporated into muscle tissue rather than body fat when appropriate resistance exercise or activity is included, and total daily calories are appropriate.
- Targeted to all athletes, and is particularly suited for youth, collegiate, and professional athletes since it is NCAA approved and NSF Certified for Sport (NSFCS).
- As a supplement, FirstString can help maximize a growing child's overall growth and development potential, including height, activity preparation, daily recovery, and athletic potential. A healthy and important addition to the diet of youth athletes to make them better on the field and in the classroom as it supplies valuable proteins and calcium and can be conveniently used as a great tasting "delivery system" for often missed but sorely needed developmental nutrition (fruits, milk, vegetables, etc.,) by adding desired contents to the mix i.e., enjoyable "smoothies."

Unique Features

- CHO content satisfies the necessary profile for maximizing protein synthesis while fitting into a "low sugar" claim, which will appeal to prevailing perceptions and preferences.
 - 2 scoops: 21 g of protein, 45 g of CHO and only 3 grams of sugar
- Sophisticated ideal blend of the highest quality fast and extended acting proteins.
- No aspartame or lactose and relatively low in sodium.
- Co-factors ensure nutrient uniformity and stability with great taste and easy mixing.
- No gas or bloating as is common with other protein powders.
- As with all dotFIT products, FirstString is designed in a synergistic relationship with all other dotFIT products and a person's traditional food intake. dotFIT powders are NOT spiked with unnecessary nutrients. Most other products in this space (e.g., bars, shakes, ready-to-drinks, etc.) are heavily spiked with many nutrients that can lead to undesirable levels within the body when combining multiple manufacturers, products, and normal food intake.
 - When consuming only dotFIT products as directed with one's normal daily food intake, the recipient is assured of keeping the body at a safe and optimal nutrient level.
- NCAA approved CHO/protein product and NSF Certified for Sport (NSFCS), which is an additional product guarantee for drug tested athletes. Click <u>here</u> for the dotFIT NSFCS section.
- Formulated and manufactured for great taste and pleasing texture in a regularly inspected NSF Certified facility, in compliance with Good Manufacturing Practices (GMPs) exclusively for dotFIT, LLC.



Nutrition Facts

32 servings per container Serving size 2 Scoops (77g)			
	0003	119]	
Amount per serving Calories	2	290)
		% D	aily Valu
Total Fat 3g			49
Saturated Fat 1g			59
Trans Fat 0g			
Cholesterol 45mg			159
Total Carbohydrate 45g	J		169
Dietary Fiber 0g			09
Total Sugars 3g			
Added Sugars 0g			
Protein 21g			429
Sodium 230mg			10%
Vitamin D	0.5	mod	2%
Calcium	200	mcg mg	15%
Iron		mg	11%
Potassium	600		12%
Vitamin A	180	mcq	20%



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