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## Memorandum - Exercise and Metabolic Acidosis

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pH Sciences® continues research into the areas of low-grade metabolic acidosis and its impact on athletic performance, aging and certain disease conditions. This memorandum summarizes the science and data regarding acidosis during intense exercise and the current indications of Alka-Plex® capability to mitigate acidosis, improve athletic performance and shorten muscle recovery time.

### **Background Information on Intense Exercise and Acidosis**

It has long been known that intense exercise increases free proton concentration (i.e. acid) in contracting skeletal muscles.<sup>1,2</sup> Most physiology courses recognize the phenomenon as “lactic acidosis.”<sup>3</sup> Recent studies indicate that acid generation from “lactic acidosis” may be a small fraction of the total acid load during intense exercise.<sup>4</sup> When free protons are released faster than the body can dispose of them the condition is often described as “metabolic acidosis.”

Lactic acidosis and metabolic acidosis have fascinated sports medicine physiologists because the onset of acidosis is a well-recognized cause of fatigue.<sup>5,6</sup>

Numerous studies have tested the hypothesis that greater skeletal muscle alkalinity leads to greater muscle endurance. Decreases in muscle tension and inhibition of phosphofructokinase synthesis (an enzyme that is key to energy production) are directly tied to acid accumulation in the muscle tissue.<sup>7,8</sup>

The acid-base balance in the body is maintained by complex chemical, respiratory and renal processes.<sup>9</sup> The most powerful and best understood extra-cellular buffer for acute acid-base changes in the body are bicarbonates.<sup>10</sup> Sodium bicarbonate was recognized as an aid to intense exercise in the late 1920's. In the 1980's a great deal of interest focused on using sodium bicarbonate – an “acidosis mitigation theory” – to enhance exercise performance.<sup>11</sup>

Ingesting sodium bicarbonate causes frequent gastrointestinal distress and dehydration. However, it remains an interesting, relatively safe method of testing the acidosis mitigation theory of enhancing athletic performance.<sup>12</sup> The distress experienced with sodium bicarbonate loading is likely due to the large sodium load, dehydration caused by increased osmotic load to the gut and significant carbon dioxide gas production.<sup>13</sup> The United States Olympic Committee and the International Olympic Committee do not include bicarbonates on their banned substance list.<sup>14</sup>

### **Overview of Alka-Plex®**

The human body functions best when arterial blood is slightly alkaline (7.35 to 7.45 pH).<sup>15</sup> Alka-Plex® supports the body's strong buffering processes that control the acid-base balance in the body so the body is less stressed while it maintains a healthy alkaline balance. pH Sciences holds an exclusive license to a group of proprietary technologies and alkalizing compounds it is branding as “Alka-Plex®.” Issued and pending patents cover its uses and the technology required to produce Alka-Plex®.

Normal body functions, such as healing processes, athletic performance and muscle recovery from intense exercise, are optimized when the body maintains healthy arterial blood pH. Alka-Plex® helps the body

**“Optimal living through healthy body pH”**

maintain optimum acid-base balance in a natural way with less stress and longer than previously thought possible. My assignment is to explore the impact of Alka-Plex® on health, longevity, vitality, stamina and muscle recovery.

Alka-Plex® can be delivered in granules, tablets, capsules, topical lotions and water.<sup>16</sup>

### **Contrasting Bicarbonates and Alka-Plex® as Ergogenic Supplements to Mitigate Acidosis**

Sodium bicarbonate, potassium bicarbonate and Alka-Plex® are strong alkalizing agents. All are GRAS (“generally regarded as safe”) a U.S. Food and Drug Administration (FDA) classification. All similarity ends there. Laboratory tests comparing the titration curves for Alka-Plex® granules and bicarbonates in 2.0 pH hydrochloric acid (similar to conditions in the stomach) produce some interesting contrasts.<sup>17</sup>

1. Alka-Plex® granules release the alkalizing agents in two gradual releases whereas the sodium and potassium bicarbonates are a single instantaneous alkaline release.
2. The first gradual Alka-Plex® release takes about 15 minutes and raises the pH of hydrochloric acid to 6.0. This is about the same initial acid neutralization as sodium bicarbonate. Potassium bicarbonate is weaker. Sodium and potassium bicarbonates raise the pH of hydrochloric acid in less than 30 seconds.
3. A second gradual AlkaPlex® release takes about one hour to raise the pH of hydrochloric acid to 6.8 (7.0 is neutral). The pH scale is logarithmic which makes the change from 6.0 to 6.8 pH very significant. Sodium and potassium bicarbonates have no such second release.
4. This second release is very gradual and does not appear to impact digestion in the stomach. The current hypothesis is that the small granules coat the stomach wall and intestinal mucosa layers so the alkaline ions diffuse through the mucosa into the epithelial tissue and blood stream.
5. Bicarbonates produce carbon dioxide gas while neutralizing hydrochloric acid which, if released in the gut, produces significant discomfort. (Alka-Plex® seldom produces gaseous discomfort.)
6. The same weight of AlkaPlex® removes about 7x more free H<sup>+</sup> ions than sodium bicarbonate and removes about 9x more free H<sup>+</sup> ions than potassium bicarbonate. Alka-Plex® is a gentler release. It is also significantly more potent than bicarbonates and has none of the negative side effects.
7. The gradual release of the AlkaPlex® alkalizing agents results in greater absorption in the blood over a longer period of time without negative side effects.
8. The hydroxyl ions (OH<sup>-</sup>) in AlkaPlex® are transported and absorbed through the small intestine more readily than the bicarbonate ion (HCO<sub>3</sub><sup>-</sup>) due to the much smaller ion size and more gentle release of the AlkaPlex® ions. The intestinal tract is dense with potassium channels that transport both potassium and hydroxide ions. The unique construction of the Alka-Plex® granules also has the additional benefit of improving hydration, not causing dehydration like bicarbonates.

Alka-Plex® can be delivered orally in granules, time-release tablets, capsules and in superior hydrating waters without the negative side effects of bicarbonates. As a result, Alka-Plex® appears to be a good candidate to mediate acidosis and should produce significantly better results than bicarbonates to improve athletic performance.

### **How Is Alka-Plex® Likely to Improve Athletic Performance?**

Studies of bicarbonate loading before athletic performance, anecdotal evidence gathered at pH Sciences and independent laboratory tests provide insights into the potential for Alka-Plex® as a tool for acidosis mitigation and enhanced athletic performance:

**Anaerobic Exercise / 1 to 7 minutes:** Exercise requiring maximum oxygen uptake for a period of 1 to 7 minutes show improved performance with acidosis mitigation techniques.<sup>18</sup> Mitigating acidosis also shows significant increases in time to exhaustion (typically a 20% improvement) with anaerobic activities.<sup>19</sup> Test subjects using Alka-Plex® regularly report improved stamina, greater endurance and increased total work accomplished. Acidosis mitigation with bicarbonates has also improved athletic speed in trained runners by a significant 2% to 3% in 800 meter races.<sup>20</sup> For trained athletes, this is a “record-shattering” improvement. Alka-Plex® is likely to have similar results without the troubling gastrointestinal side effects.

**Aerobic Exercise / 10+ minutes:** Exercise requiring less than maximum effort for 10 minutes or longer has not shown uniform results with bicarbonate loading. Some acidosis mitigation results, such as those performed at the Harvard Fatigue Laboratory, showed 20% to 30% improvements in runs lasting 15 minutes.<sup>21</sup> Several prominent anaerobic exercise studies of bicarbonate loading did not find similar results in the later stages of aerobic exercise.<sup>22,23</sup> Another well-documented double blind, placebo controlled aerobic exercise test measured a 14% increase in total work output during a 60 minute bicycle test for acidosis mitigated subjects.<sup>24</sup> The longer release time with Alka-Plex® and the improved digestive comfort may be able to replicate or improve on those results. Researchers are loath to make any definitive statements about the effectiveness of bicarbonate loading during aerobic work.<sup>25</sup> The Company may wish to examine additional delivery systems, such as gels, for endurance sports.

**Interval Exercise:** Repeated bouts of exercise, with each bout separated by a brief rest period, have shown the greatest, most consistent improvement in performance associated with acidosis mitigation techniques.<sup>26</sup> For example, cycling with four 1-minute maximum sprints, followed by 1 minute rest intervals, produced a remarkable 42% improvement in time to exhaustion with acidosis mitigated subjects in a double-blind, placebo controlled study.<sup>27</sup> Similar results are reported in numerous tests and subjective reporting on the sensation of fatigue confirm that acidosis mitigated test subjects do not “feel” as fatigued even after exceeding their usual limits.<sup>28</sup> Alka-Plex® may be a useful product for elite athletes in their training regimen.

**Recovery Time:** Test subjects using Alka-Plex® as an acidosis mitigation technique during training and participation in endurance sports consistently report shorter recovery time, less muscle soreness and improved muscle healing. This is especially seen in reducing soreness and stiffness the day after marathon or century bicycle rides. One of the consistent indications from interval training described in the previous paragraph is that acidosis mitigation makes the muscles ready for more exertion after a brief rest. This phenomenon is an area for more research building off the strong anecdotal evidence being compiled at pH Sciences.

### **What Are Other Likely Areas of Interest for Alka-Plex® to Mitigate Acidosis?**

Intense exercise causes acute stress on the acid-base balance. Other stressors include excess dietary acids in foods, which has been documented to lead to chronic, low-grade metabolic acidosis.<sup>29</sup> Chronic, low-grade metabolic acidosis is also associated with aging.<sup>30</sup> The increase in H<sup>+</sup> ions among the aged is tied to the normal decline in renal function.<sup>31</sup> Similarly, physiological aging of the lungs also impacts the acid-base balance.<sup>32</sup> Finally, prescription drugs and trauma can also induce acidosis.<sup>33</sup>

We are all living longer. Chronic, low-grade metabolic acidosis is perceived as normal as we age. So what are the consequences of this acidic stress? What are the implications for future uses of Alka-Plex®?

Acid-base homeostasis exerts a major influence on protein function, thereby critically affecting tissue and organ performance.<sup>34</sup> For example, certain enzymes (which are proteins) function effectively in a very narrow pH range. The body's homeostatic response to acidic swings is very efficient and blood pH is usually maintained within a tight "normal" range.<sup>35</sup> It's just that "normal" gets more acidic as we age.<sup>36</sup> These efficient, compensatory mechanisms become severely stressed as we age and lead to a progression of debilitating conditions often linked to aging such as kidney stones, renal disease, bone disease and similar conditions.<sup>37,38,39</sup>

Even the loss of muscle mass associated with the aged appears to be linked to increasing acidity in the aging body.<sup>40</sup> Only more recently has scientific research begun to establish the relationship between chronic, low-grade metabolic acidosis, aging and a wide range of chronic diseases often associated with aging.<sup>41,42</sup> Even mild degrees of low-grade acidosis, such as that occurring by ingesting a high animal protein diet, are being linked to endocrine system changes, hormone insensitivity, hypo-thyroidism and hyperglucocorticoidism.<sup>43,44</sup>

The implications for Alka-Plex® are profound. There are no accepted or even effective treatments for low-grade metabolic acidosis.<sup>45</sup> The effectiveness of Alka-Plex® can most easily be proven in the sports field. I recommend that Alka-Plex® be established as an effective method to mitigate acidosis in sports medicine before moving on to more traditional medical or health maintenance applications.

Most importantly, Alka-Plex® is safe. The U.S. FDA has reviewed the Alka-Plex® ingredients and has issued two letters recognizing the ingredients as GRAS. The products have shown no significant negative side-effects and Alka-Plex® has passed a Stanford Research Institute acute oral toxicity test in which rats were given 100x the standard daily dosage.<sup>46</sup> It is likely that the product, Alka-Plex®, can receive GRAS designation pursuant to FDA guidelines.

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