

amino scope®



KYOWA HAKKO BIO'S NEWS FROM AROUND THE GLOBE • FALL 2018



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New York
Times
BESTSELLER

GENIUS FOODS



Become Smarter, Happier, and More Productive
While Protecting Your Brain for Life

MAX LUGAVERE

WITH PAUL GREWAL, MD



Cognizin® & Sports Nutrition

Sports Nutrition and the Brain.

The sports nutrition market is growing every year, with the US sports nutrition market projected to reach \$11.9 billion by 2021.

Optimal performance is a combination of both nutrients for muscle building and healthy cognitive function which plays an important role in motor control, decision making, coordination, reaction time and other cognitive tasks that are essential during exercise and sports activity.

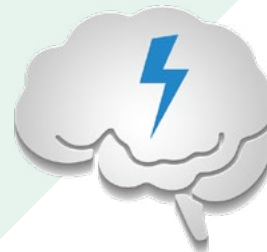
Athletes that encounter unpredictable or dynamic situations and movement in competitive sports depend on clear focus and quick decision-making. This need has led to an increase in the inclusion of nootropics – cognitive function improving ingredients – in sports nutrition products with the aim of raising awareness of the importance of mental alertness in physically-demanding sports.

One of these nootropics is Citicoline, CDP-choline. Citicoline is a vital ingredient for the synthesis of phospholipids including phosphatidylcholine, a major constituent of brain tissue. Citicoline has been historically used in the treatment of stroke patients in Japan and was then introduced as a prescription drug in European countries.

Kyowa Hakko has manufactured Cognizin®, a branded form of Citicoline, for dietary supplements in the US since the early 1980s and obtained Novel Food Regulation status in Europe in 2014. The efficacy of Cognizin® is clinically proven and shown to provide nutritional support for brain energy and support focus and attention in healthy people.

Studies, across a spectrum of audiences, have demonstrated the positive cognitive health benefits of Cognizin®:

- An increase in brain energy among middle-aged adults was observed when 500mg of Cognizin® was taken daily for six weeks.



- A significant reduction of omission and commission errors among middle-aged women conducting computer tasks was observed when consuming 250mg/day of Cognizin® for 28 days.



- A notable effect on attention was observed among adolescent males when consuming 250 or 500mg/day of Cognizin®. In this study, the Ruff 2 & 7 Speed Task test and motor speed of the finger-tapping tests were conducted to evaluate muscle control, motor ability and psychomotor performance.

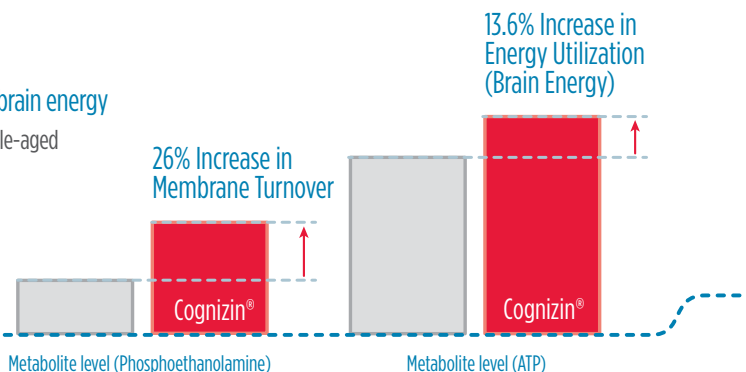
Although there are several nutrients and supplements for healthy brain function on the market, considering the results of multiple clinical trials, Cognizin® is a beneficial ingredient for people participating in sports.



Cognizin® Citicoline's effect on cellular synthesis and brain energy

Researchers observed increases in brain activity among middle-aged adults who had taken 500mg Cognizin® for six weeks*1

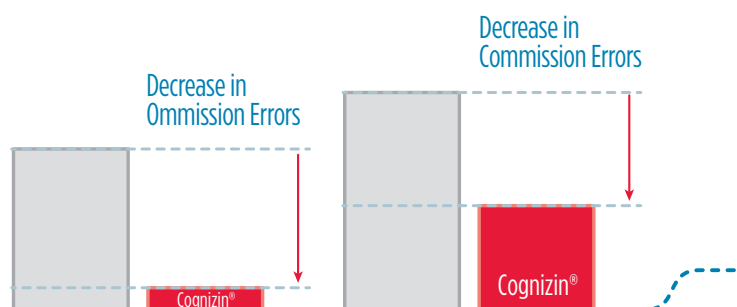
■ Placebo
■ 6 weeks@500mg / day Cognizin®



Cognizin® Citicoline's effect on focus and attention

Cognizin® at 250mg / day improves attention and focus in middle-aged women*2

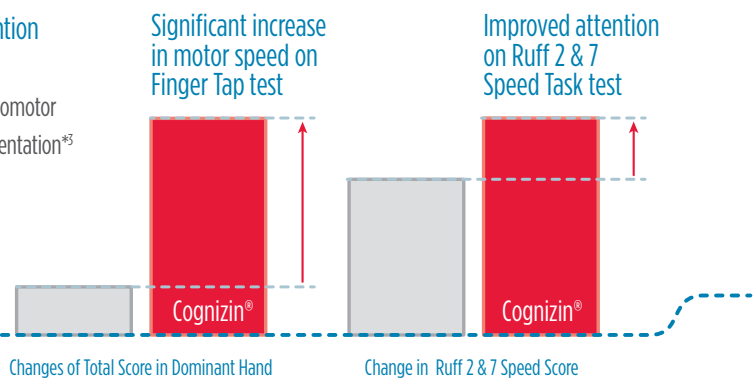
■ Placebo
■ 4 weeks@250mg / day Cognizin®



Cognizin® Citicoline's effect on motor speed and attention in adolescent males

Researchers observed an increase in both attention and psychomotor speed in adolescent males after 28 days of Cognizin® supplementation*3

■ Placebo
■ 28 days@250mg or 500mg / day Cognizin®



1. Silveri MM et al. Citicoline enhances frontal lobe bioenergetics as measured by phosphorus magnetic resonance spectroscopy. *NMR Biomed.* 2008; 21(10):1066-75.

2. McGlade E. et al., Improved Attentional Performance Following Citicoline Administration in Healthy Adult Women. *Food and Nutrition Sciences.* 2012;3:769-773.

3. Yurgelun-Todd D et al. The Effect of Citicoline Supplementation on Motor Speed and Attention in Adolescent Males. *Journal of Attention Disorders.* 2015; 1557-1246.

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References:

- 1) Passport, Sports nutrition: Drivers and prospects, July 2017
- 2) International Journal of Sport Nutrition and Exercise Metabolism, 2018, 28, 200-211
- 3) Nutritional Outlook: Brain Health Nootropic Supplements Growing in Sports Nutrition, April 2018, Volume 21-Issue 3
- 4) *NMR Biomed.* 2008; 21(10):1066-75.
- 5) *Food and Nutrition Sciences.* 2012;3: 769-773.
- 6) *Journal of Attention Disorders.* 2015; 1557-1246
- 7) *Balkan Med J.* 2013 Jun; 30(2): 167-171.

Cognizin®

For the evolution of your mind®

BioKyowa

Threading Together Quality from Start to Finish

Quality is key in order to produce and deliver the best possible product to our customers. From receiving raw materials all the way through to shipping the final product, quality is woven into the fabric of BioKyowa. Many different departments are working together, interlaced like a favorite quilt, each committed to the quality of the end product. If one small piece of the quilt does not fit together, just right, the imperfection is obvious.



BioKyowa has three departments that emphasize the importance of quality and perform checks within their department to ensure that quality standards are being met. These departments are Quality Assurance, Quality Control and The Quality and Logistics department. Each of these three departments is responsible for specific parts of the process.

Quality Assurance

The Quality Assurance department considers themselves to be the customer's advocate. The quality management system is much like the initial plan for putting together the quilt. Each piece of the system

must be in place and must be followed with the utmost care to reach the goal of producing the highest quality product. From issuing and managing documentation, to determining root cause analysis and corrective action to releasing product, the Quality Assurance department takes the lead for the company and sets the standard high for our customers.



Quality & Logistics department

Quality Control

In the Quality Control department, analysis is performed on raw materials, in-process samples, and finished product samples to ensure that quality is "built into" the product from the beginning to end. Just as each square is checked for size and uniformity to ensure homogeneity and consistency for the overall finished quilt, each and every piece

of equipment and technique must be operated and performed with the highest precision and accuracy to ensure our product is safe and correct for our customers. From receiving samples into the laboratory to the analysis that is performed, each step of preparation and testing is done with the customer in mind and the knowledge that our job is key in preventing potentially unsatisfactory product from reaching those it is intended for.



Quality and Logistics

The Quality and Logistics department is responsible for the receiving of raw materials, delivery of raw materials, and the shipment of finished products. Just as you would inspect and select the perfect fabric and thread for your quilt, raw materials for our processes are chosen based on our quality guidelines and upon receipt of raw materials many quality checks are performed.

These checks include inspection of the shipping container, verification of seals, inspection of the raw material itself, and raw material testing.

Each of these checks is important to verify BioKyowa is receiving the best raw materials. After these checks are complete and the raw material is received into the warehouse it is tracked all the way to the finished product.

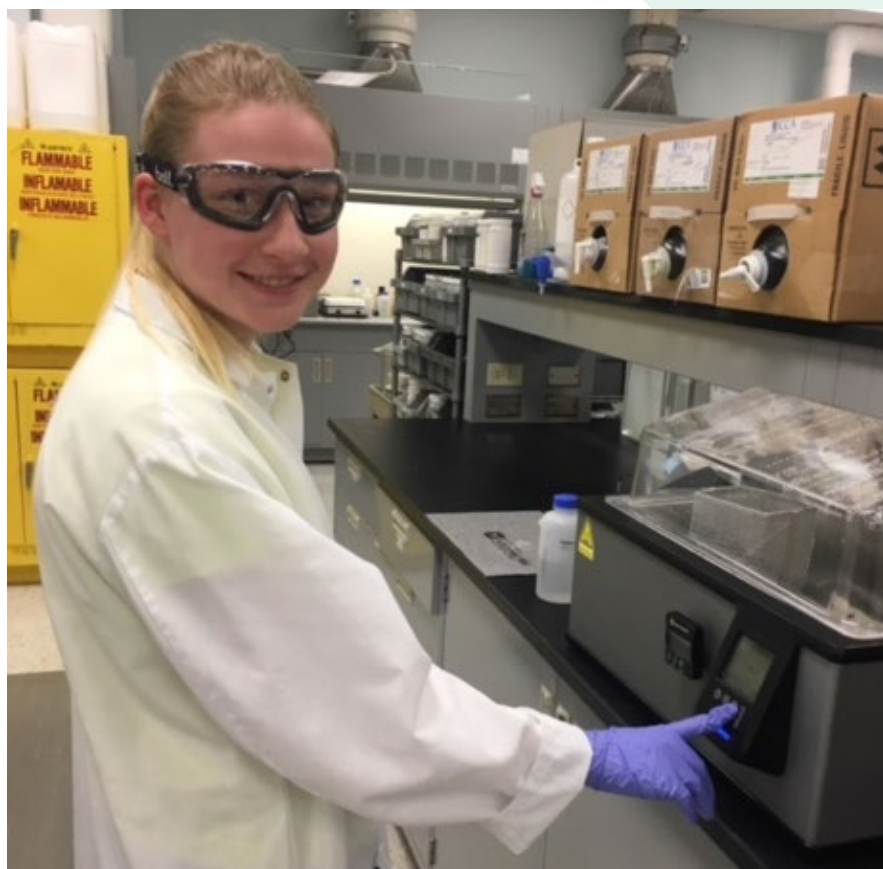


When product leaves BioKyowa, it has been through rigorous testing from the Quality Control department.

A full in-depth review of all documentation associated with the product has been performed by the Quality Assurance department, and the Quality and Logistics department has conducted a stringent shipping process in order to ensure all customers receive their purchased products in great condition. When finishing a quilt, this is where any loose threads or unhemmed pieces are corrected.

The shipping process includes several checks of the product, packaging, and shipping containers in addition to an electronic inventory management system to ensure only the best product is shipped to our customers.

From start to finish, raw material to finished product shipping, quality is our mission and our customer's full satisfaction and health is our number one priority.



US PR Events

Exploring the role of Setria® Glutathione for Healthy Lifestyles

Two recent “Master Classes” held at Project Farmhouse in New York City provided the perfect environment for an educational forum on the power of “Master Antioxidants” and the role that glutathione plays in immunity and detoxification as part of healthy aging.

In her opening remarks, Keri Glassman explained why glutathione is called the “Master Antioxidant”. “Glutathione not only neutralizes free radicals by itself, it also has the ability to reactivate other antioxidants, such as vitamins C and E. After antioxidants like vitamin C and E neutralize free radicals, they become unstable radicals themselves. Glutathione helps recycle these unstable molecules, returning them to active duty and extending their abilities to scavenge for and neutralize oxidants.”

As a registered dietitian and nutritionist, Keri always recommends



Setria® Glutathione Master Class
with Keri Glassman, MS RN, CDN

that a diet should be the key source of nutrition, but in reality, busy lifestyles often prevent this. So, a little additional “health insurance” through supplementation can make all the difference. The audience was encouraged to pick their top glutathione rich food from a list of the top six. Asparagus was number one, followed by avocado, spinach, oranges and lastly walnuts!

Delving deeper into healthy lifestyles and the role glutathione plays, Keri took the participants through two specific functions:

Immunity: The immune system is a system of cells that work in the body to destroy pathogens and cancerous cells. Glutathione contributes to the stimulation of natural killer cells, increases white blood cell count and neutralizes free radicals while helping to regulate apoptosis.

Detoxification: Glutathione helps eliminate toxins, chemicals and potential carcinogens made their way into the body and that have

become absorbed. It is most abundant in the liver and the kidneys, the primary detox and elimination organs. It also protects the DNA against damage or mutation caused by harmful chemicals, environmental agent or damaging lifestyle habits.

While your body’s systems come equipped with a complex set of mechanisms and compounds designed to eliminate toxins, your body can continually absorb more through food, water and air. Ridding your body of common toxins can help increase energy levels, boost your immune system, and it promotes healthy aging and overall wellness.

“Glutathione is present in every cell of the body, but as we age glutathione levels decrease due to various factors including UV irradiation, alcohol, cigarettes, drugs and chemicals,” commented Keri. “It’s important that we top up our glutathione levels to ensure that we get the protection this master antioxidant can provide.”



Kyowa Hakko, a global manufacturer of research-backed Setria® Glutathione, conducted a study on glutathione which found that daily consumption of glutathione

supplements was effective at increasing the amount of glutathione in the human body by up to 35 percent when taken daily at a dose of 1,000 milligrams for six months.

“I really enjoyed the presentation. I never realized what a powerhouse glutathione was and how important it is especially as a woman who is now over 40. It’s something that I’m really going to take into account in my daily regimen and especially in advising others.”

*Solana Nolfo
Master Class Attendee*

It is Never too Early for Brain Health Choices: Why to Care Now

According to author and committed brain health advocate, Max Lugavere, changes in the brain begin decades before the first symptom of mental decline is detected. For that reason, it’s become his driving passion to spread the word among young people about the critical links between the brain and the food we eat.

As part of an interview, which took place on September 6th at New York University’s Skirball Center, Lugavere explained that the same food and dietary patterns that can help stall mental decline, can also help your brain work better in the here and now.

During the event, hosted by investigative science journalist Nina Teicholz, Lugavere discussed that it was his mother’s mental decline that motivated him to write *Genius Foods*, answering various questions

from the audience including what foods to avoid in a regular diet. Lugavere recommends avoiding grain seed oils, such as canola, seed, corn and soy oils, cultivated modern grains and fruits, and also added sugars — which are problematic because they keep insulin chronically elevated. He instead recommends avocados, and puts eggs, particularly the yolk, at the top of his “Genius foods” list because they are high in a myriad of nutrients that benefit the brain. Grass-fed beef and greens like kale, spinach and arugula are also on his list.

Although Lugavere would like to think that we can get all the nutrients that we need from food, he explains that this is “not the case in the modern world,” leading him to incorporate exercise, as well as different supplements, into his daily diet. Lugavere explained that one of the reasons he’s a fan of supplementing with Cognizin® Citicoline “is because Citicoline is a naturally occurring nutrient found in the brain.” Citicoline increases an important substance



in the brain called phosphatidylcholine that is critical for healthy brain function.

Cognizin®, the branded form of Citicoline, has been researched and shown to support focus, attention and mental energy.* The event was sponsored by Cognizin® Citicoline, which is made by a patented fermentation process and manufactured by Kyowa Hakko. With 1 in 7 younger people complaining about retaining information and developing a competitive edge, Lugavere is convinced that “you are never too young or too old to make healthy brain choices.”

Tradeshows & Conferences

Kyowa at Vitafoods Europe May 15th – 17th, 2018

Kyowa Hakko Europe and Kyowa Hakko Bio Italia, the European offices of Kyowa Hakko Bio Co., Ltd., exhibited at Vitafoods Europe. Vitafoods Europe is the annual global nutraceutical event taking place in May in Geneva, Switzerland. The trade show provides visitors the chance to scout for ingredients, raw materials, food supplements as well as services to support their business.

Kyowa showcased its range of branded ingredients focusing on healthy aging with Cognizin® Citicoline, Setria® Glutathione and on sports performance with Sustamine® L-Alanyl-L-Glutamine and Setria® Performance Blend.

A New Approach to Enhance and Sustain Nitric Oxide Availability

Karen E. Todd, a Registered Dietitian, Certified Health & Fitness Specialist and the Sr. Director of Global Brand Marketing for Kyowa Hakko U.S.A. presented a 30 minute session on Kyowa Hakko's novel blend 'Setria® Performance Blend.' Setria® Performance Blend has been formulated to enhance and sustain Nitric Oxide availability before and after exercise and meant to target athletes looking to maximize muscle output and achieve better strength-training results, while reducing fatigue and speeding muscle recovery.

Setria® Performance Blend is a patent-pending combination of Kyowa Hakko's own Setria® Glutathione and L-Citrulline. L-Citrulline is an amino acid which research



has demonstrated to increase Nitric Oxide (NO) production. NO is a gas molecule that encourages blood vessels to relax, allowing for a better influx of oxygen and other nutrients while training to achieve greater strength and performance. Glutathione, a master antioxidant, helps to prevent NO degradation. Research shows that combining L-Citrulline and Setria® Glutathione helps sustain NO production more than either alone.

Kyowa Hakko manufactures its products by a patented fermentation process which ensures the ingredients are pure and safe, non-animal derived, containing no additives, artificial flavors or preservatives.

Vitafoods Insights and Trends:

- Natural sources for vitamins and minerals are gaining more and more importance.
- Continuing an ongoing trend, "natural" and "organic" were words often found in ingredients and products.
- Brands are investing more in clinical research to support the health benefits of their products.

- Sports nutrition continues to move mainstream, it is no longer a niche and brands are actively exploring this segment with cutting-edge sports nutrition and functional ingredient solutions delivering innovative, on-the-go functional foods and beverages targeted to active consumers.

Consumer Trends:

- Prevention rather than treatment approach to mental support and food supplements for inner beauty.
- Products and ingredients have added value if they are from a natural source, organic, without artificial colors or flavors, without preservatives, non-animal derived, etc. => products that consumers can trust.
- Consumers are demanding different delivery formats e.g. by using confectionery as a delivery format for nutraceuticals.

Vitafoods™
Europe



Kyowa at Innovation Seminar and Supplier Expo Complementary Medicines Australia (CMA) May 2nd, 2018

Kyowa Hakko Bio Singapore participated in its 1st Australian event this past summer, the Complementary Medicines Australia, Innovation Seminar & Supplier Expo.

Situated along the famous Sydney Harbour, this event focused on educating delegates on topics of innovation within the complementary medicines industry under the theme “Tomorrow’s Ideas... Today”. The 1-day event was attended by more than 150 delegates, ranging from manufacturers, raw material suppliers, distributors, government officers, consultants to healthcare professionals.

Karen E. Todd, a Registered Dietitian, Certified Health & Fitness Specialist and the Sr. Director of Global Brand Marketing for Kyowa Hakko U.S.A. gave a presentation on ‘The Power of Prevention: Supporting Healthy Aging with Setria® Glutathione’. It covered the antioxidant benefits of glutathione and how it is important for healthy aging, which aligns to Australia’s current market trends.

The purpose of this event was to promote awareness and educate the delegates about Setria® Glutathione, after its approval by TGA in 2014.

Kyowa’s “Exploring New Horizons for Setria®” March 20th, 2018

This past spring, Kyowa Hakko Bio Singapore Pte Ltd organized an intimate and private seminar in Manila: Exploring New Horizons for Setria®. The event targeted local manufacturers of health food



supplements and personal care products.

In the Philippines as well as in South East Asia as a whole, L-Glutathione Reduced—colloquially known as “Gluta”—is a popular supplement ingredient for skin whitening and has a market quantity of at least 10MT. In fact, it is so popular many cosmetic companies included it in their topical products even though the reduced Glutathione is not stable in such formulations.

More than 40 Filipino manufacturers attended the event to learn about the new sciences of Setria® for skincare as well as AquaGluta®—a liquid stable solution for RTDs and topicals that are already in the market. Participants included well known beauty market leaders in the Philippines such as Intelligent Skincare.

The event was joined by a panel of international speakers – Ms. Karen E. Todd (United States), Ms. Yuki Nakamura (Japan), and Ms. Cicilia Amex (Singapore). Participants reported coming out of the event with better technical and formulation understanding using Setria® and AquaGluta®.

Upcoming Events



Integrative Healthcare Symposium
February 21-23, 2019
New York, New York



Oregon Suppliers Night
February 25, 2019
Portland, Oregon



Nutraceuticals Expo
February 27-28, 2019
Madrid, Spain



Southern California IFT
Suppliers' Night Expo
March 6th, 2019
Anaheim, California



Expo West
March 7-9, 2019
Anaheim, California



DCAT Week
March 18-21, 2019
New York, New York



FIBO Global Fitness
April 4-7, 2019
Cologne, Germany



CPhI North America
April 30-May 2, 2019
Chicago, IL



Vitafoods Europe
May 7-9, 2019
Geneva, Switzerland



Japan—Headquarters

Kyowa Hakko Bio Co., Ltd.

North & South America

Kyowa Hakko USA

Europe

Kyowa Hakko Europe GmbH

Kyowa Hakko Bio Italia S.R.L.

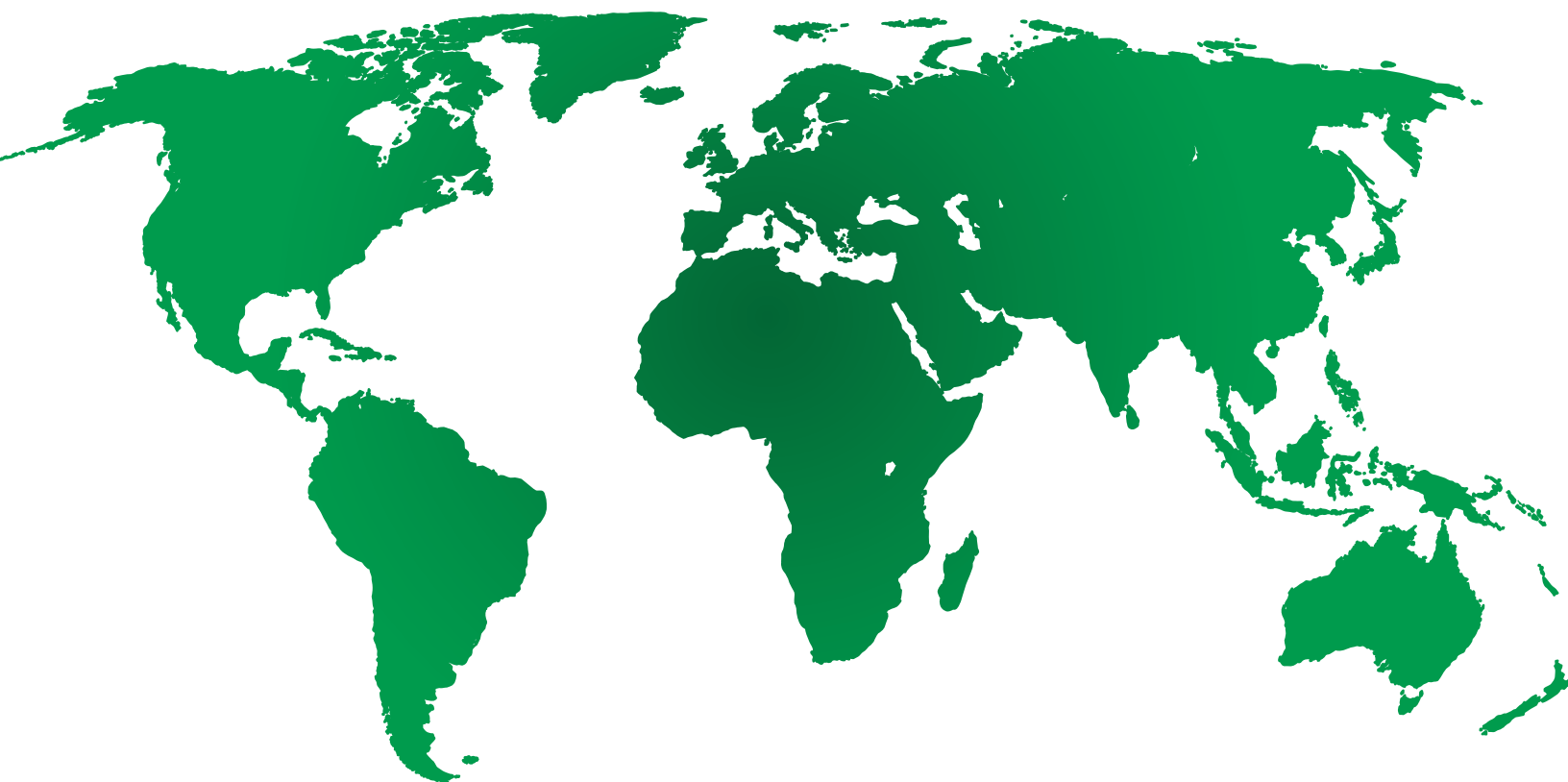
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