

# amino scope<sup>®</sup>



KYOWA HAKKO BIO'S NEWS FROM AROUND THE GLOBE • FALL 2019





We, Kyowa Hakko Bio, were spun out from Kyowa Hakko Kogyo's biochemical business unit and are a wholly owned subsidiary of Kirin Holdings Company, Limited.

Taking advantage of our state-of-the-art fermentation technologies, Kyowa Hakko has made substantial contributions to the health and well-being of people around the world by commercializing an array of useful chemical substances, including various amino acids, nucleic acid-related substances, vitamins, bioactive substances, pharmaceutical products, as well as oligosaccharides and dipeptides.

The global demand for high-value amino acids has recently increased, due in part to rising levels of healthcare in emerging countries, as well as new needs being generated by customers not only in specialty markets, but also in domestic and overseas markets for generic drugs. Given our intent to better serve customers by offering quality products in a timely manner, Kyowa Hakko Bio plans to reinforce its technological development, and supply for realizing a stronger global production and sales system.

In inheriting the valuable assets, manpower, and engineering prowess accumulated over 50 years since the invention of the glutamic acid fermentation process and setting a high goal of "organically combining fermentation and synthesis" based on this legacy, our renewed company is committed to developing a wide variety of innovative products, and providing medicines and dietary supplements for the better health and well-being of people worldwide.

Your continued support and contribution is greatly appreciated.

**Takeshi Minakata**

President and Chief Executive Officer  
Executive Director of the Board



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# The Latest on Cognizin® Citicoline

## Promising Combination of Cognizin® and Omega-3

**Prevalence of age-related** cognitive health impairments has become a common issue shared among aging societies these days. Growing demand and research developments in this field has expanded the brain health market, which is expected to surpass USD \$5.8 billion in 2023 at a 9% CAGR.<sup>1</sup> In addition, increased awareness about health benefits of supplements for enhancement of attention, focus and memory among younger generations has now become another driving force for this market.

**One of these** supplement ingredients aiming to support cognitive health, also called nootropics, is Citicoline, CDP-choline. Citicoline is a substance naturally found in every cell of our body and a vital ingredient to brain health for the synthesis of phospholipid including phosphatidylcholine, a major constituent of cellular membrane of brain tissue and

neurons. Citicoline is also converted to acetylcholine, a neurotransmitter. Both of these compounds play significant roles in various neuronal function. Our clinical studies have shown that orally digested citicoline helped to boost brain energy as well as improved focus and attention in healthy individuals.<sup>2, 3, 4</sup>

**Phosphatidylcholine** is the most abundant cellular phospholipid, which is synthesized from citicoline and fatty acids including omega-3, such as docosahexaenoic acid (DHA). Due to its unique structure, DHA enhances cellular membrane fluidity which supports smooth brain communication. It is widely believed that brain DHA level decreases with aging<sup>5</sup> and deficiency of DHA in the brain is related to a decline in cognitive function. However, we cannot synthesize them in our body and we do not intake enough DHA from foods. Thus many individuals may benefit from supplementation of DHA.

**Both Citicoline and DHA** are vital ingredients as components of brain tissue and neurons. While citicoline has shown to be beneficial for enhancing brain energy and cognitive performance, DHA support brain communication via increased membrane fluidity. Combining citicoline and DHA may have further synergistic benefits for improving learning and memory ability.<sup>6</sup>

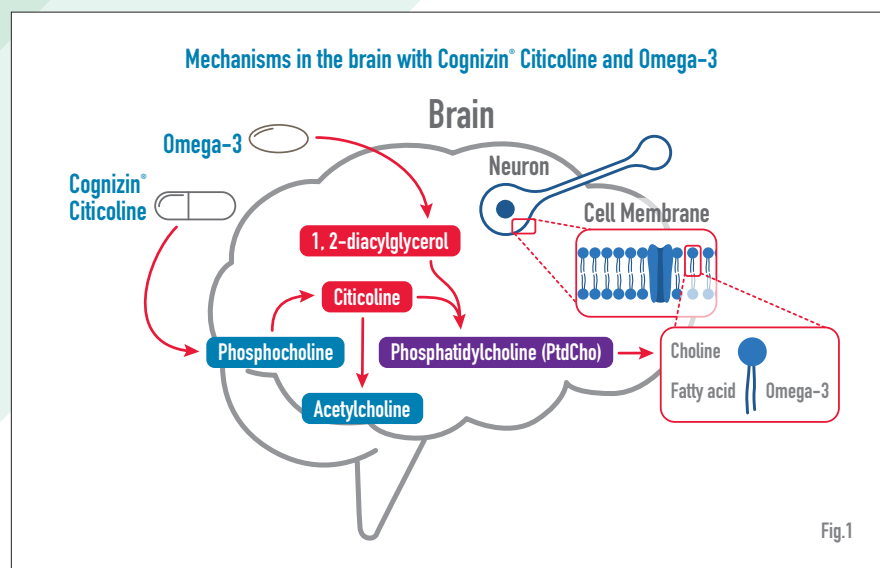
1. Future Industry Insight "Global Brain Health Supplements Market: Opportunities and Forecasts, 2017-2023"
2. Silveri MM et al., *NMR in Biomedicine*. 21(10): 1066-75, 2008
3. McGlade E et al., *Food and Nutrition Sciences*, 3: 769-773, 2012.
4. McGlade E. et al., *J Atten Disord*.23(2):121-134, 2019
5. Youdim KA et al. *Int J Dev Neurosci*. 18(4-5):383-99,2000
6. Nakazaki E et al. *J Pharmacol Sci*.139(4):319-324, 2019

## eSports, Nootropics & Cognizin

The world of eSports has been all the rage recently, and for good reason. According to video game market research firm Newzoo, the eSports market will for the first time, exceed the billion-dollar revenue mark in 2019 with a year-on-year growth rate of 26.7%. (fig.2)

Furthermore, global eSports tournaments are also quickly approaching viewership numbers that rival professional sporting events such as Wimbledon and the Super Bowl. (fig.3)

Increased popularity and investment in eSports is raising its global awareness and gamers in this realm are seeking supplements that power their brain through long and intense hours of gaming and provide them





## 2019 ESPORTS REVENUE STREAMS/GLOBAL

Including Year-on-Year Growth

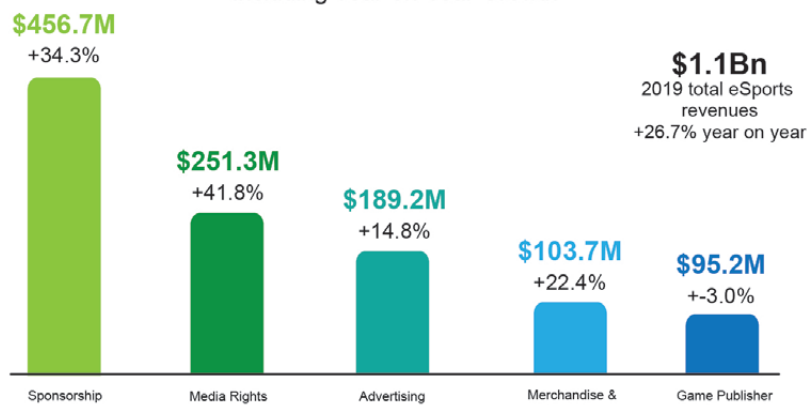


Fig.2

## ESPORTS VS SPORTS Viewership Numbers

### ESPORTS

League of Legends Worlds  
**201 Million**  
Dota 2 The International  
**14.96 Million**  
IEM Katowice 2018  
**1.48 Million**  
Overwatch League Playoffs  
**1.23 Million**

### SPORTS

Rio 2016 Summer Olympics  
**3.6 Billion**  
Fifa World Cup  
**3.572 Billion**  
Super Bowl LIII  
**98.2 Million**  
Wimbledon  
**56 Million**

Fig.3

increased attention and focus, all the while avoiding crashes energy drinks tend to give. Smart supplements, or what they are commonly known as, nootropics, are gaining recognition for their ability to provide the type of mental boost that gamers need to achieve optimal performance.

Citicoline is one of these nootropics that naturally occurs in the body's cells and is especially vital to brain health and cognitive function. Cognizin®, a branded form of Citicoline, is clinically proven to provide nutritional support that benefits mental processes, focus and concentration, as well as healthy brain metabolism. In fact, 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. This type of benefit is ideal for gamers looking for a competitive edge since nootropic drugs, such as Ritalin and Adderall, are banned from eSports leagues.

A combination of a healthy diet and supplementation is key for optimal performance and Cognizin® has been demonstrated to positively impact cognitive ability. It helps users stay sharp and maintain focus, effects which are especially beneficial to gamers.

### Sources:

1. Newzoo: Global Esports Economy Will Top \$1 Billion for the First Time in 2019
2. Hotspawn: Esports vs Sports: How the Two Compare by The Numbers
3. NMR Biomed. 2008; 21(10):1066-75
4. Food and Nutrition Sciences. 2012;3: 769-773
5. Journal of Attention Disorders. 2015; 1557-1246

## US Nootropic Market: Cognizin® Awareness Continues to Grow



Max Lugavere, Brain Health Expert Reveals The Truth Behind Brain-Hacking & Nootropics

On July 23rd at the Roxy Cinema in New York City Max Lugavere took the stage for a live recording of his Genius Life podcast, now the #1 rated podcast on iTunes. Max was interviewed by Jason Bosley-Smith, MS, LDN, CNS, FDN to talk brain hacking, brain health and nootropics.

Nootropics has surged across vast consumer markets in recent years, sparking interest in what they are, how they work and what brain-hacking really means. Max explained in his interview "We all want to become smarter, better, faster and more mentally agile, so for me, foods are one of the best ways to 'hack your brain' – but there are other ways to as well, including resistance training, sleeping, meditating, and taking the right nootropic supplements to help support focus, attention and mental energy" he says.

cont. on next pg.

Nootropics vary in their function, with some promoting immediate “brain power” results while others function to promote long-term brain health. “From innocuous levels of caffeine to prescription attention medication, the umbrella of nootropics is too large to give a one-size fits all definition,” notes Lugavere. “Not all nootropic supplements are created equal, and this is something I learned when learning about Kyowa Hakko’s branded ingredients. When you stick to a brand name, it’s sort of like getting a better version of your favorite toilet paper as opposed to a supermarket brand.”

Cognizin® is the branded form of Citicoline and can be found in different nootropics targeted for specific brain health benefits. Unlike other ingredients, Cognizin® isn’t chemically synthesized, it’s made by an innovative fermentation process to yield high-quality and purity. It’s backed by research and is clinically studied to support mental energy, focus and attention.

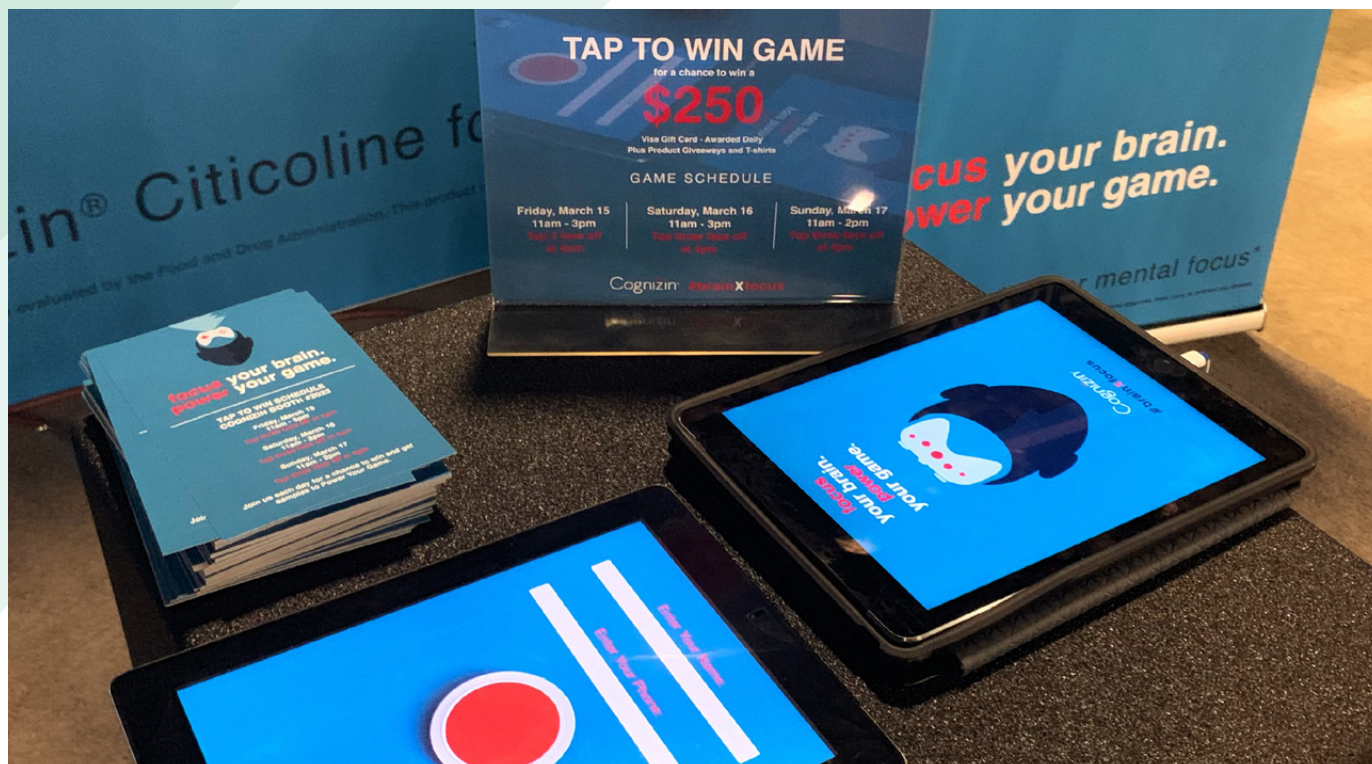


### Cognizin® Featured for the first time at SxSW Expo

Kyowa Hakko USA headed to Austin, TX in March to feature Cognizin®, the branded form of Citicoline clinically studied to support mental energy, focus and attention, for South by Southwest (SxSW) Gaming Expo as interest in nootropics continues to grow in the gaming industry.

Competition was fierce at the SxSW Gaming Expo and gamers are really looking to up their games. A recent study using the Finger Tap Test supported improved attentional abilities, psychomotor speed and inhibition in health adolescent males when supplementing with Cognizin® Citicoline over a 30-day period (McGlade, et al., 2015). The double-blinded study was conducted by neuropsychologist using a variation of test which simulated cognitive functions similar to those exercised in PC videogames.

Cognizin® sponsored two popular PC games at the event-Hearthstone, an online card logic game and PlayerUnknown’s Battlegrounds (PUBG), an online multiplayer battle royale game. Kyowa Hakko USA also featured finished products and information on Cognizin at their exhibition booth. Consumers were really excited to learn the benefits of Cognizin as the ingredient and be part of our Finger Tap competition.





# Kyowa Hakko Bio & Kirin Holdings

*Kirin Holdings Company, Limited (hereinafter, "Kirin Holdings") concluded that, at a meeting held on February 5, 2019, the Board of Directors resolved that Kirin Holdings acquires 95% of all outstanding shares in Kyowa Hakko Bio Co., Ltd. (hereinafter "Kyowa Hakko Bio") from Kyowa Hakko Kirin Co., Ltd. (now "Kyowa Kirin").*

## Purpose of the Share Acquisition

Kirin Holdings has aimed to co-achieve sustainable growth with societies by addressing social issues through its businesses and realizing value creation for the customers under its "New Kirin Group Vision 2021" long-term management vision for 2021 by utilizing its unique business portfolio, centered on the Alcoholic and Non-Alcoholic Beverages businesses and the Pharmaceutical and Bio-Chemicals businesses, as well as its strengths in technology and marketing. The Kirin Group identified "Health and Well-being", "Community engagement", and "the Environment" as CSV priority issues, and expects new value creation by addressing "Health and Well-being" issues through its businesses to be one of potential growth drivers of the Kirin Group.

The Kyowa Hakko Kirin Group companies, which are in charge of the Kirin Group's Pharmaceutical and Bio-chemicals businesses, possess the Management Philosophy "to contribute to the health and well-being of people around the world by creating new value through the pursuit of advances in life sciences and technologies." In accordance with this philosophy, its businesses cover Bio-Chemicals and other



businesses around the core Pharmaceutical business. Kyowa Hakko Bio was established in 2008 by Kyowa Hakko Kogyo Co., Ltd. (now Kyowa Kirin) as a spin-off of the Bio-Chemicals business. As the subsidiary of the Kyowa Hakko Kirin Group companies responsible for the Bio-Chemicals business, it has leveraged its wide-ranging knowledge of fermentation and synthesis to supply a variety of products, such as amino acids, nucleic acids, vitamins, peptides and synthetic compounds to customers in Japan and overseas, providing goods and services that meet the health needs of people around the world.

Kirin Holdings and the Kyowa Hakko Kirin Group have been facilitating collaboration with each other. For example, in 2017, "iMuse" was launched by Kirin Holdings as a group—wide brand to commercialize the "Lactococcus lactis strain plasma," which has been the fruit of joint development between three companies of Kirin Company, Limited, Koivai Dairy Products Co., Ltd., and Kyowa Hakko Bio. Against the

backdrop, as a result of considering and discussing the possibility for further collaboration in the business domain of "Health and Well-being" on which Kirin Holdings is focusing as a future growth driver, Kirin Holdings and Kyowa Hakko Kirin came to the decision that by making Kyowa Hakko Bio a direct subsidiary of Kirin Holdings, it would be possible to more effectively use each other's strengths and management resources, as well as raise the speed of business development, beginning with the "Health and Well-being" domain, and so open the way to maximizing group synergies and the corporate value of Kyowa Hakko Bio. In addition, the Share Acquisition would allow Kyowa Hakko Kirin to concentrate management resources on the Pharmaceutical business, primarily new drug development, and to further accelerate the pace of growth, leading in turn to the maximization of corporate value of the Kirin Group. Accordingly, it was decided that part of the Kyowa Hakko Bio shareholding would be sold to Kirin Holdings.

# 35 Years of BioKyowa

*BioKyowa is Kyowa's US-based manufacturing facility. With continuous operations in Cape Girardeau, MO starting in 1984, BioKyowa is celebrating 35 years of providing quality ingredients to Kyowa customers in the US and abroad. BioKyowa has been fortunate enough to have dedicated employees from the very start – here are some stories of those employees that have been with BioKyowa from the beginning.*

## KENNY ROSS

*Employee since 1984*



I was hired in 1984 at the age of twenty. We began with class room training for 6 months and then testing for competence. I was placed in fermentation as a field operator. At the time, there were two fermentation field operators on each shift; one operator ran the field and the other one ran the lab doing Lysine HPLC analysis and sugar analysis.

After two years of being a fermentation operator, I transferred to the maintenance department. Not long after starting in maintenance I married the love of my life in 1986 and we purchased our first home in Kelso. I worked as a maintenance technician for nine years (1986-1994). Our first son, Duncan, was born 1993.

I began attending night class to learn electronics; this helped me to promote into the I/E department. I worked with this department for two years (1995-1996). During this time our second son, Cole, was born in 1995. My next adventure was when I was offered the opportunity to be a shift supervisor. I accepted and shortly after becoming a shift supervisor our third son, Devin, was born in 1997.

As the shift supervisor, I was responsible for eight operators on rotating days and nights 12 hour shifts. I enjoyed this position from 1997-1999. In 2000, CG-7 plant expansion began and I was offered the position of Plant 1 Extraction Superintendent. Plant 1 was producing feed grade Tryptophan and Threonine at the time. The job of Plant 1 Extraction Superintendent became the most challenging job thus far in my career with BioKyowa. This has been my position from 2000 to current. It entails overseeing the extraction process as well as the packaging of final product.

Since the beginning of CG-7, we went from only producing two crude grade amino acids to currently producing six different crude grade API amino acids. On top of a busy career, my wife and I purchased another 86 acre farm adjacent to our existing farm and a small cabin at Kentucky Lake. Needless to say I have my hands full at home as well.

My career at BioKyowa has come with many challenges and rewards. My latest undertaking is taking on the position of Assistant Production Manager. I plan on utilizing my past experience in order to rise to the challenge of continuing to help this

company prosper until my retirement in 2025.

## DAVE JENNINGS

*Employee since 1984*



When asked to write an article describing my 35+ year history with BioKyowa, I had to pause and think about what aspect I should write about.

Should I talk about the history of the plant and the changes to the facility that have occurred over the years?

To starting the plant up to manufacture the amino acid L-lysine, the first plant in the U.S. to manufacture lysine by a continuous fermentation production method. The conversion of utilizing molasses as a sugar source that was brought in by barge up the Mississippi River, to a much cleaner corn syrup brought in by rail to reduce our environmental impact and improve yield. The expansion of the plant to include two new facilities to produce L-Tryptophan and Nucleic Acid. And ultimately the closure of the lysine production facility and a halt to Nucleic Acid production. The re-birth of the plant, to become a manufacturer of high-end amino acids that are supplied to the world. The many upgrades and improvements over the years to the fermentation, extraction, utility and environmental operations for



better performance, yield, safety and conservation.

Should I talk about my personal experiences at the facility? Working with the startup team from Japan to make the production of L-lysine in the U.S. become a reality. As a production supervisor you are always faced with many challenges to overcome; shift work in general which can always make any task more difficult, dealing with fermenters and evaporators that were outside in freezing conditions, the many facility goals that were achieved and the few that were not. Overseeing the extraction section to help improve productivity and increase yield which proved to be rewarding and demanding. The opportunity to visit Japan and learn about the culture and operations at the Hofu plant. Working in the engineering section to help with the expansion of the facility and the many equipment additions that were going to be necessary. Safety and Environmental to meet regulatory compliance for an increasing amount of programs being introduced by OSHA and the EPA.

And finally, overseeing the environmental department which requires an increasing amount of attention to maintain regulatory compliance and help reduce our environmental footprint. To meeting the many individuals, Japanese and American, which have worked and visited the plant over the years, sometimes for as little as a few days and for some many years as well.

Throughout it all there has been one common denominator, and that has been BioKyowa. Whether you are talking about the experiences gained through the variety of jobs, the witness to change in technology and methodology of the facility over the years, or the growth of a family, BioKyowa has been that one common denominator.

**DAVE ROARK**  
*Employee since 1984*



I will celebrate my 36th year of working at BioKyowa in January. My first job at BioKyowa was Fermentation operator, and I then worked in the Maintenance Department for the next 20+ years before starting in the Project Department.

In those 36 years I have seen a lot of changes. We have had 5 different plant managers and 7 different company presidents. Our first product that we made was feed grade Lysine and now we are making 15 different amino acids as industrial, API intermediates and food grade products. Another change at BioKyowa is safety. Safety is now the most important item of any job at BioKyowa. Looking back at May of 1984 when we started the manufacturing process in the Lysine plant we should consider ourselves fortunate that we did not have a serious accident resulting in a major injury or worse.

The safety culture at BioKyowa has changed for the better. We must make sure that everyone is on board with safety. We use the STOP program, which is a safety behavior program and it is working very well. No single program will keep us a 100% accident free company. That's why we must keep reinforcing to every employee to work safe not only at work but at home. The next big change is how much attention is paid to the quality of our products. We have people assigned to preventing foreign material

issues, doing risk assessments on equipment, HACCP tours, internal process audits, food safety program, ICH Q7 and the list goes on. The point I am making is; we take quality very serious at BioKyowa.

**BRAD WILSON**  
*Employee since 1985*



I have seen many changes over the years at BioKyowa and those changes have enriched my life and many others working in this plant. I joined the company in March of 1985 over 34 years ago and have experienced continuous change ever since. Production processes, Quality improvements and Safety are some of the main components improved many times over from talented individuals with ideas and a desire to improve this facility.

Continuous change has shaped BioKyowa into a modern state of the art facility. I have seen a continuous fermentation process change to an innovative batch process. BioKyowa has evolved from a single feed grade (Lysine) manufacturer to producing multiple food and crude grade amino acids. Many changes have been made to our laboratory, warehouse, utilities and waste treatment areas to improve efficiency and meet the highest quality standards. These changes have been made possible due to the safety, dedication and support of all employees and staff working together as a team over the years.

# PR Events

## Beauty From Within Market Booms in US

In August, International Beauty Expert Corinne Morley spoke at a press luncheon at The Press Lounge in New York City, covering the booming interest in wellness infused beauty that has taken off industry wide.

Morley, who has extensive experience in the beauty industry, including holding impressive roles at Estée Lauder and Trilogy Natural Skincare, spoke to the modern meaning of 'beauty from within' – noting that while this is not a new concept, consumers and retailers alike, including Sephora, Nordstrom and Anthropologie, are beginning to blur the lines between health supplements and traditional beauty products on shelves.

"Beauty is much more than skin-deep, it's a reflection of how we're feeling," explains Morley, "Everything that we do externally and internally affects the outward appearance of our skin. It's not just about how we treat the outer surface of our skin, it's also a reflection of what's going on inside—from lack of sleep, to stress, from diet, to too much sun exposure, from environmental toxins to what skincare products we choose to use, everything has an impact."

Morley notes that one of the skin's biggest enemies is "the environment that we live in," informing the key beauty media and influencers in attendance that "without a doubt" free radicals, found in our everyday environment, are "one of the most negative influences on how our skin looks and behaves."



*Beauty Expert  
Corinne Morley  
(center) and guests.*

Free radicals are unstable molecules that cause damage to DNA in cells, disrupting normal cell function, while also having the power to deteriorate the skin's structural support by decreasing its suppleness and elasticity. While free radicals are in our environment every day and are part of the natural aging process, Morley explains that "certain things actually stimulate free radical activity, such as air pollution, UV radiation, smoking, alcohol and poor nutrition, so we want to calm the free radical activity...because we know how damaging it can be to our health, wellness, and how our skin is going to age."

"Luckily," continues Morley, "there is an antidote-antioxidants. Antioxidants are powerfully combative toward free radicals, because they help neutralize them."

Glutathione, known as the body's 'master antioxidant,' is found, to varying degrees, in all cells, tissues, body fluids and organ systems in the body. Glutathione can neutralize potentially harmful free radicals, eliminate toxins, chemicals and

potential carcinogens absorbed in the body, and can reactivate other antioxidants that are important for skin, hair and nail health like Vitamin E. However, glutathione levels may decrease due to various factors such as age, diet, UV exposure, health conditions, weight, medications, and poor lifestyle habits. Supplementing with glutathione and incorporating glutathione-rich foods into your diet may help raise glutathione levels in the body\*. Setria® Glutathione, a patented form of Glutathione, is a branded ingredient that has been clinically researched to help increase the body's stores of glutathione, and can help support immunity, detoxification, and skin brightening\*.

'Wellness and beauty go hand-in-hand, and research is the cornerstone of both,' states Morley, "Setria® Glutathione is great because now, customers are really demanding quality, research-backed ingredients. This ingredient, is found in many supplement products for beauty, detox, immune health and recovery.



# Europe Market Update



## European Customer Event in Milan

In early September Kyowa Hakko Bio Italy (KHIB) hosted in Milan an event for customers, channel partners and distributors from all around the Mediterranean region, Middle East and Ukraine.

The focus of the event was to share Kyowa's philosophy, talk about current product lines and Kyowa branded ingredients.

The event was opened by Nicola Urso, VP of KHIB, with a warm welcome and introduction to the day's agenda. Oksana Ritchie, European Marketing Manager, presented the majority of the materials taking the audience deeply into the science behind Kyowa's current product offering in these territories.

In addition, she also provided an overview of market trends in areas such as eye health, gut health, immune system support, cognitive health and sports nutrition. Cognizin, Setria and Sustamine were all extensively discussed including the introduction of the latest studies.

The event was well attended and from the feedback given was very well received with partners particularly mentioning how much better they now understood the Kyowa approach and philosophy. In addition to the presentations all attendees were also invited to tour Kyowa Hakko Bio Italy's warehouses in Milan for both pharma and food ingredients.

## Goodbye and Welcome

On a separate note the European division of Kyowa Hakko said goodbye to its President in July with Mr. Shimazu returning to Japan. On behalf of everyone in Europe we thank him for his contribution over the previous 5 years and wish him continued success in the future.

At the same time, we are very happy to welcome Mr. Takeuchi, the new President of Kyowa Hakko European divisions. Mr. Takeuchi already has an in-depth understanding of the European market and its culture having worked in Kyowa Hakko Bio Italy for a number of years. No doubt he will be able to confidently lead Kyowa's further growth in the European region.

## Upcoming Events



**Chicago Section IFT Suppliers Night**  
November 6, 2019  
Rosemont, Illinois



**CRN Annual Conference**  
November 6-9, 2019  
Carlsbad, California

## Society for NeuroSports

*from lab bench to weight bench*

**The Society for NeuroSports Conference**  
November 14-16, 2019  
Deerfield Beach, Florida



**Nutraceuticals Expo**  
March 4-5, 2020  
Madrid, Spain



**Southern California IFT Suppliers' Night Expo**  
March 5, 2020  
Anaheim, California



**Expo West**  
March 3-7, 2020  
Anaheim, California



**DCAT Week**  
March 23 - 26, 2020  
New York, New York



#### 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.

#### China & South East Asia

APEC (except Japan)

Kyowa Hakko Bio, Singapore Pte., Ltd.

Kyowa Hakko Bio India Pvt., Ltd.

Kyowa Hakko (Guangdong), Pharmaceutical Co., Ltd.

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#### More Upcoming Events



##### FIBO Global Fitness

April 2-5, 2020

Cologne, Germany



##### SupplySide East

April 21-22, 2020

Secaucus, New Jersey



##### CPhI North America

May 5-7, 2020

Philadelphia, Pennsylvania



##### Vitafoods Europe

May 12-14, 2020

Geneva, Switzerland



##### ISSN Annual Conference and Expo

June 18-20, 2020

Daytona Beach, Florida



##### IFT

July 12-15, 2020

Chicago, Illinois



##### NBJ Summit

July 27-30, 2020

Carlsbad, California