

What can be expected from this technology

Contribute to the brain health of people around the world in the fields of food & beverages to pharmaceuticals

Citicoline is a compound found in the body

Citicoline is needed for the maintenance of cell membranes in the brain and neurons

Cell membrane damage and quality deterioration as a result of trauma to the brain and aging

Decline in brain function



Maintenance of brain function

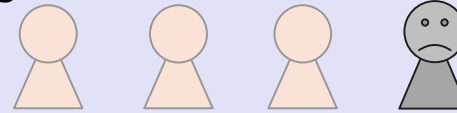


Kyowa Hakko Bio's citicoline

Global market needs and main applications

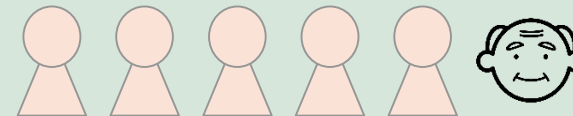
Number of stroke victims:
13.7 million*

Chances of having a stroke:
one in four people over the
age of 25.**



An ingredient for active pharmaceutical ingredients

65 years and older in Europe and the US: 18%,*** about one in six.



An ingredient for health foods

*World Stroke Organization "Learn about stroke"

** N Engl J Med. 379(25):2429-2437 (2018)

*** World Population Prospects 2019

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Pharmaceutical use as treatments for brain disease

■ For the patients

- Use as a treatment for stroke*
- Other benefits
 - Brain dysfunction from accidental trauma**
 - Glaucoma treatment ***
- A wide range of dosage forms, including injections, oral formulations and eye drops

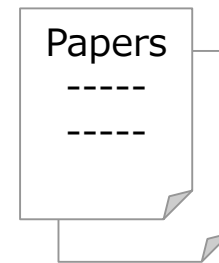
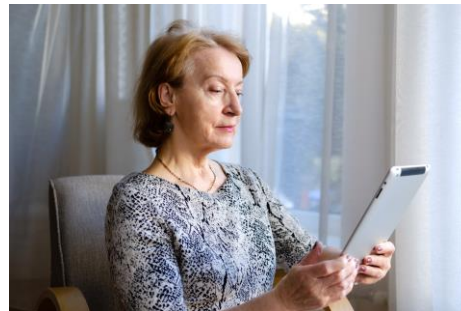


*Curr Opin Investig Drugs 2(12), 1757-1762 (2001)
**From the Drug Interview Form
***Nutrients 12(3), 793 (2020)

Health foods to **maintain** cognitive decline

■ For the middle-aged and elderly

- Support for improving cognitive function as it declines with age
- Studies on the effectiveness of citicoline for the elderly has been published in academic journals****



****Methods Find Exp Clin Pharmacol 19(3), 201-210 (1997)

Use in **food and beverages** to support brain power and skills

■ For young and mature customers

- Helping those who want to improve their work performance and efficiency
- Can be widely applied to convenient beverages and processed foods



Focus

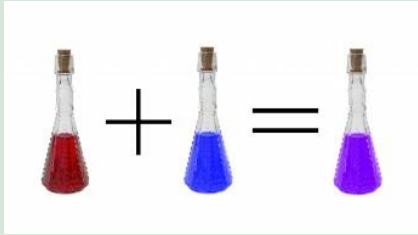


About this technology

Technology overview 1: established an innovative method for the mass production of citicoline based on an unique technology

Challenges of past technologies

The main technique used was chemical synthesis



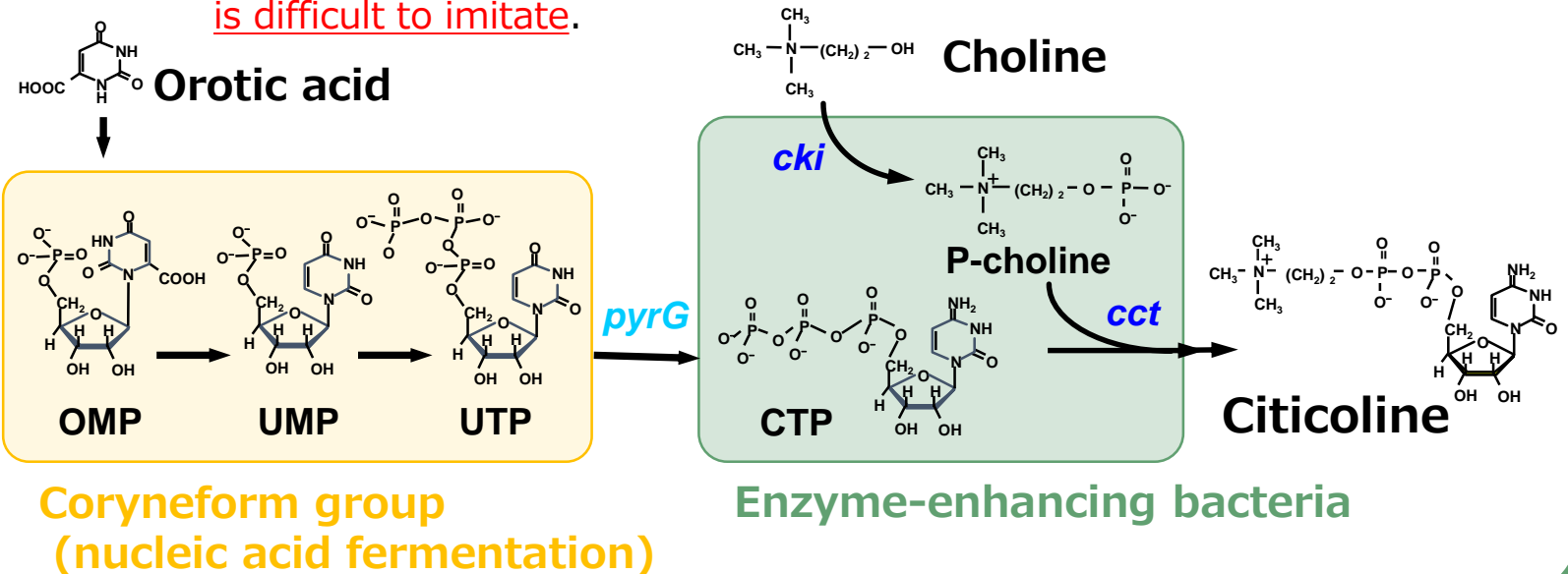
Expensive, low-volume production

Difficult to ensure a steady, low-cost supply of citicoline for wide population



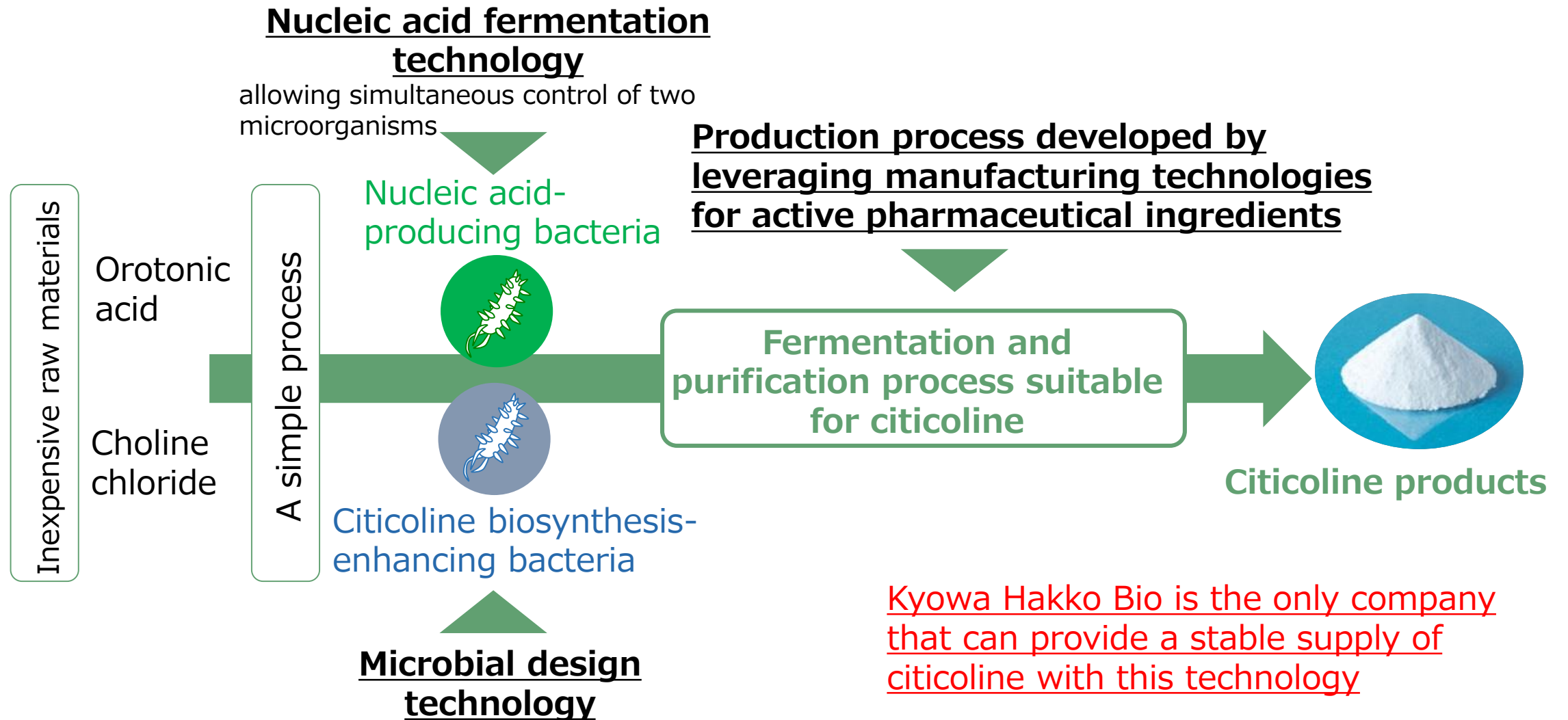
What Kyowa Hakko Bio has made possible

- We have designed an original process combining the nucleic acid fermentation technology developed over many years and microorganisms with enhanced enzymatic activity
- We have established a process that enables high quality product manufacturing in a plant scale
- Kyowa Hakko Bio, with its extensive knowledge of microorganisms, is uniquely able to provide citicoline inexpensively and in large quantities by using a production method based on its established know-how that is difficult to imitate.



About this technology

Technology overview 2: a biological process combining conventional and new technologies



About this technology

The History of Kyowa Hakko Bio and citicoline

1956

Kyowa Hakko developed the world's first microorganism-based amino acid fermentation technology

1970s

Citicoline produced via chemical synthesis began to be distributed on the world's markets as a pharmaceutical product

1990

Kyowa Hakko Bio began producing citicoline through fermentation

2003

Kyowa Hakko Bio started to actively promote citicoline under brand name Cognizin

2016

Cognizin has been introduced to a major, well-known health food brand in the US.

2016-2020

Demand for energy drinks is on the rise
Citicoline's concept - improved attention and concentration - meets market needs

Future

We are planning to expand areas where Cognizin can be used as a food ingredient

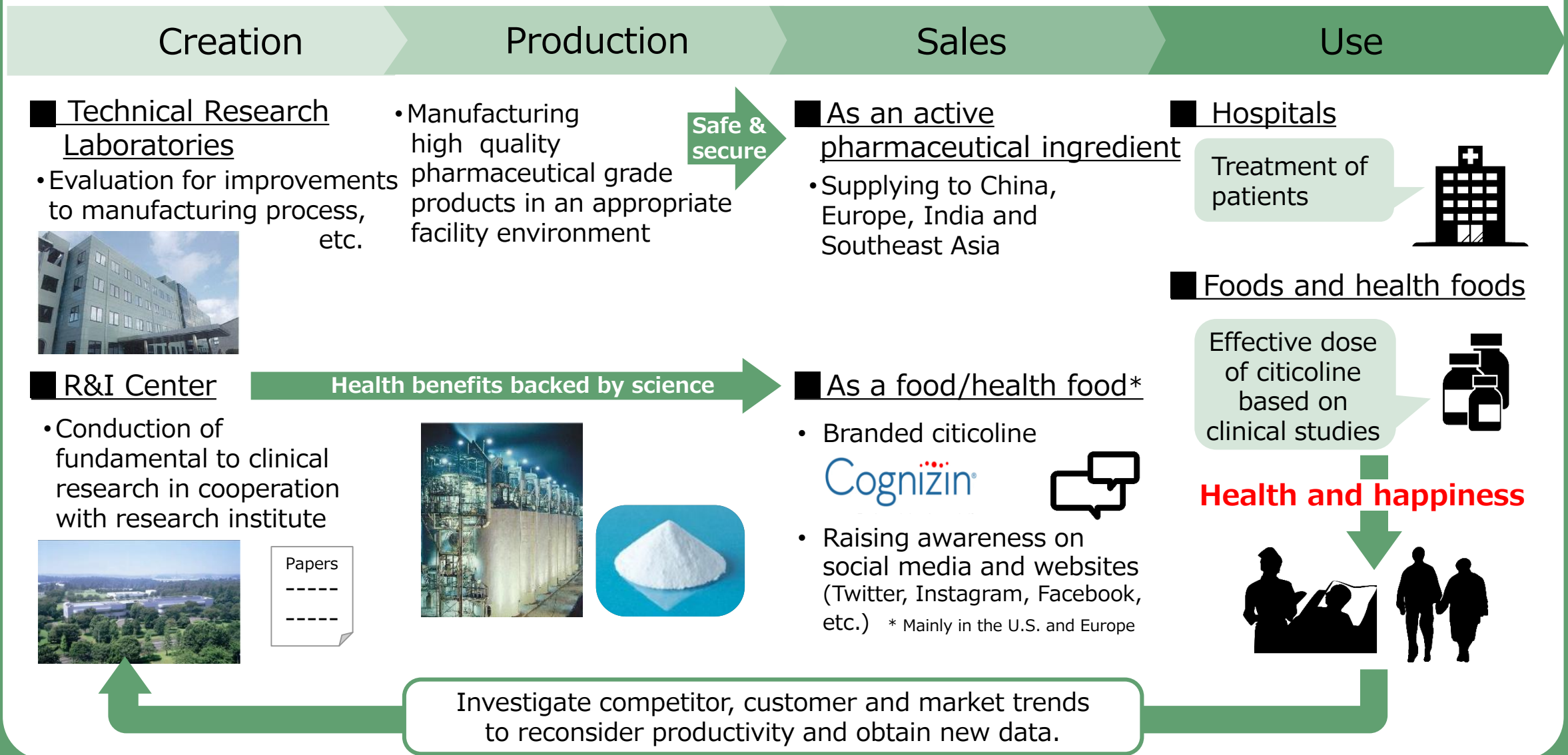


Cognizin®
For the evolution of your mind®



The uniqueness of this technology


Provide added value in the form of citicoline produced by Kyowa Hakko Bio





■ As an active pharmaceutical ingredient


- Supplying to China, Europe, India and Southeast Asia

■ As a food/health food*

- Branded citicoline 
- Raising awareness on social media and websites (Twitter, Instagram, Facebook, etc.) * Mainly in the U.S. and Europe



■ Hospitals
Treatment of patients 

■ Foods and health foods
Effective dose of citicoline based on clinical studies 

Health and happiness



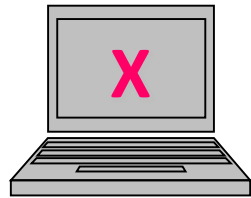
Investigate competitor, customer and market trends to reconsider productivity and obtain new data.

Uniqueness of this technology

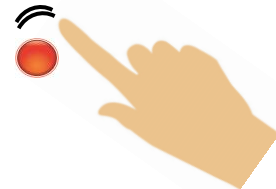
Effectiveness and application of citicoline scientifically proven by Kyowa Hakko Bio

Examples of Effects of citicoline intake

■ Clinical trials in healthy individuals



- Decreased omission error when operating a computer*



- Improved finger tapping test ¹**

¹ Number of times a button is tapped

■ Combined with other well-known ingredients



- Combination with DHA
→ Further cognitive improvement can be expected***

* Food and Nutrition Sciences, 3: 769-773 (2012)

**J Atten Disord, 23(2), 121-134, (2019)

*** J Pharmacol Sci 139(4), 319-324 (2019) (non-clinical development)

Proposals for new markets and areas

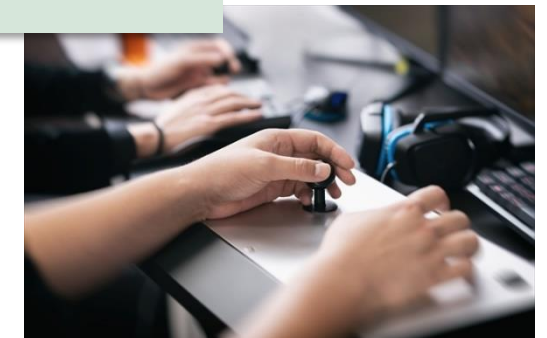
■ Providing Citicoline to people seeking better focus across generation



- Improve the work productivity of remote workers in their new lifestyle and maintain their focus

For the evolution of your mind !

- E-sports market, where finger tapping tasks and focus are important



Future vision

Contribute to support the brain health of more people

→ **Kyowa Hakko Bio provides citicoline as branded ingredient for brain health backed by scientific evidence**



Expanding the number of countries and regions where citicoline can be used as an ingredient for foods and health foods via ingredient registration procedures

Food

Food for
maintaining
health

Pharma



High-quality, safe citicoline for “pharmaceutical”, and proven Cognizin brand citicoline for “foods and health foods”