

Think clearly

Cognizin®

For the evolution of your mind®

Discover the difference
between cognitive
enhancing ingredients.



Cognizin® - Citicoline

What is Cognizin® ?

Cognizin is a brandend from Citicoline, a natural substance found in every cell of the body and especially vital to brain health.

Citicoline is broken down during intestinal absorption and, after easing through the blood/brain barrier, is reconstituted in the brain as Citicoline.

What are the benefits of Cognizin® ?

- provides vital nutrients that help the brain generate electrical impulses, care for healthy brain cells and protect neurons from free radical damage.
- aids in the synthesis and maintenance of cell membranes.
- supplies precursors for the synthesis of phospholipids, including phosphatidyl-choline, a major constituent of brain tissue.



- helps maintain normal levels of acetylcholine, a nutrient that regulates memory and cognitive function.
- support visual function.
- enhances communication between neurons.
- the brain requires tremendous amounts of energy. Cognizin - Citicoline supports the healthy mitochondria activity required for sustained mental effort.

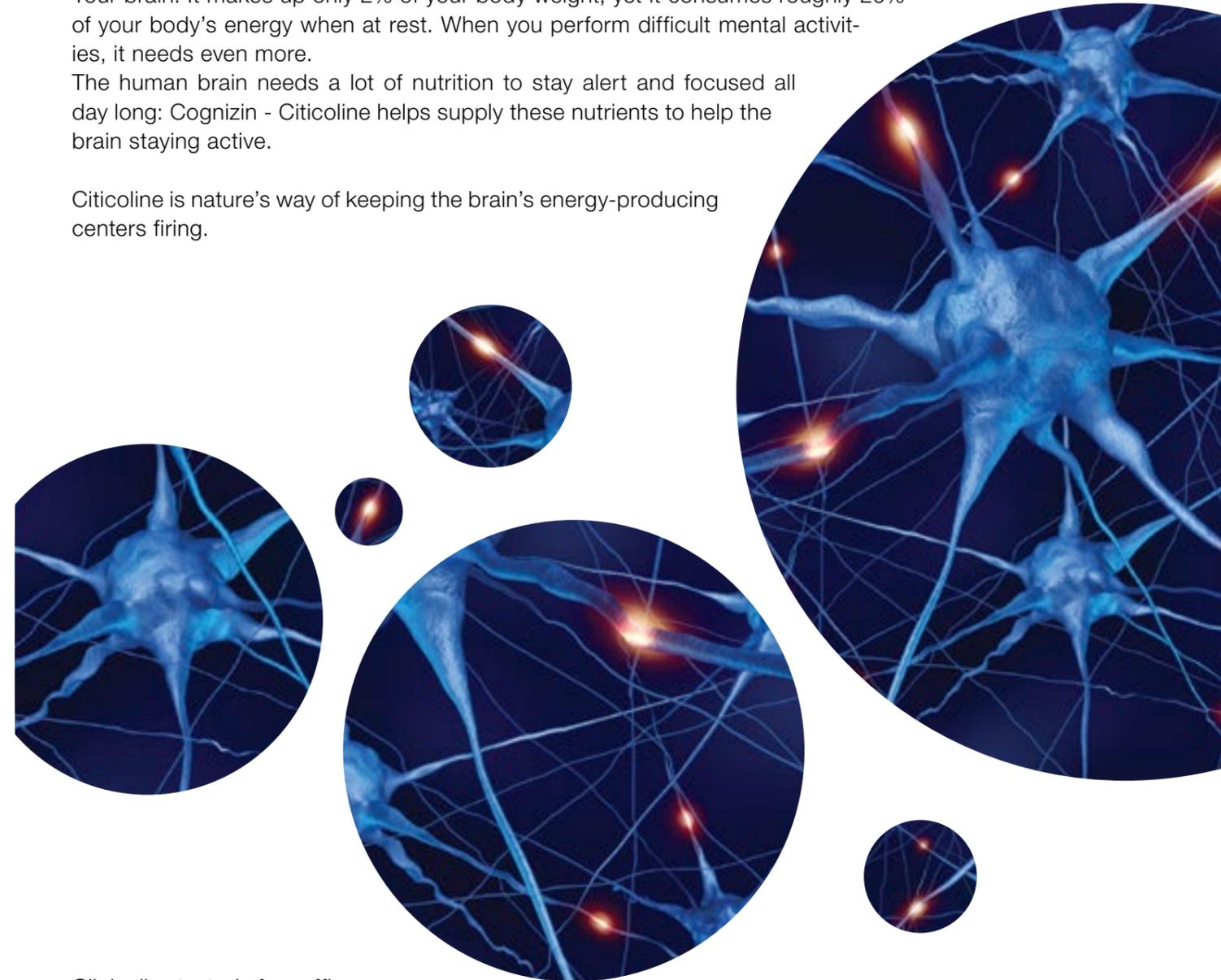
Cognizin® – Citicoline the cognition enhancer

The brain's energy consumption

Your brain. It makes up only 2% of your body weight, yet it consumes roughly 20% of your body's energy when at rest. When you perform difficult mental activities, it needs even more.

The human brain needs a lot of nutrition to stay alert and focused all day long: Cognizin - Citicoline helps supply these nutrients to help the brain staying active.

Citicoline is nature's way of keeping the brain's energy-producing centers firing.



Clinically tested for efficacy, Cognizin delivers a patented form of Citicoline that supplies your brain with the energy it needs to stay sharp.

A proprietary form of Cognizin - Citicoline is a potent brain-health nutrient that's been clinically shown to support mental energy, focus, attention and recall.

Tested in human clinical trials and developed using a patented fermentation process, Cognizin – Citicoline is a pure, allergen-free, vegetarian and GRAS ingredient that's stable and effective. For a functional difference consumers are sure to notice, add the proven brain power of Cognizin – Citicoline to your next product.

Cognizin-Citicoline is a water-soluble compound.

Replenish your mind, body and spirit.

Cognizin® and energy

Energy reserves play a critical role in healthy brain function. The first vital benefit of Cognizin - Citicoline is its ability to help keep the brain's energy-producing centers firing. While the brain makes up only two percent of a person's body weight, it consumes roughly 20 percent of the body's energy when at rest. When performing difficult mental activities, the brain needs even more energy.

Clinical research has found that Cognizin supports the health of mitochondria, the powerhouses within cells that actually produce the brain's energy. Healthy mitochondrial function results in higher levels of ATP — the body's main energy storage molecule — in brain cells.

Cognizin® and focus

The second brain-health benefit of Cognizin - Citicoline is increased focus and concentration.

The ability to focus requires:

1. An adequate ongoing supply of energy
2. Healthy communication between neurons

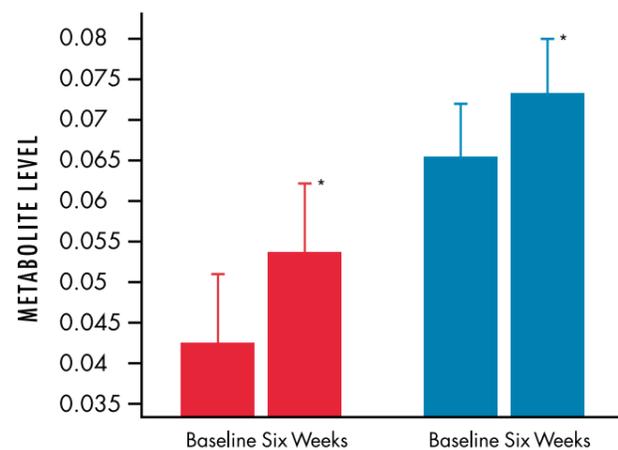
Not only does Cognizin support healthy brain metabolism, but it also aids in neural communication by protecting neural structures against free radical damage and by facilitating the transmission of information through healthy cell membranes.

To function optimally, cell membranes need adequate levels of phospholipids. Phospholipids are a combination of lipids (fats) and the mineral phosphorus that line cell membranes and help determine what is allowed in and out of the cell. Cognizin provides a water-soluble compound essential for the synthesis of phosphatidyl choline, the phospholipid that makes up approximately 30 percent of brain tissue. By increasing the body's supply of these essential phospholipids, Cognizin supports healthy brain activity.

Cognizin® and memory

Cognizin's third brain-health benefit is improved memory storage and recall. Cognizin Citicoline is often called a "brain nutrient" because it increases levels of several important neurotransmitters, including acetylcholine, an important brain chemical that regulates memory and cognitive function. Cognizin has also been shown to support the activity of nerves that respond to acetylcholine, helping to raise activity levels in the brain's learning and memory circuits.

Cognizin® Citicoline Increases Cellular Synthesis and Energy



Cellular Synthesis
26.0% ↑ PE

Cellular Energy
13.6% ↑ β-ATP

*Significant change from baseline

PE: Phosphoethanolamine
Data represent mean ± SD
metabolite ratios relative to the
total 31P signal at each visit.

Silveri, M.M. et al. Citicoline
enhances frontal lobe bioenerge
as measured by phosphorus
magnetic resonance spectroscopy
NMR Biomed. 2008; 21(10):
1066-1075. Patent Pending.



How does Cognizin-Citicoline work?

What are the primary health benefits of Cognizin Citicoline?

Cognizin is a branded form of Citicoline, a natural nutrient found in every cell of the body and especially vital to brain health. Unlike artificial stimulants that ramp up energy and attention levels only to have those levels come crashing down later, Cognizin provides nutritional support that helps:

- fuel mental processes
- enhance focus and concentration
- support healthy memory function



How does Cognizin pump up the brain's energy reserves?

Cognizin helps keep your brain's energy centers firing. Clinical research has found that Cognizin supports the health of mitochondria, the powerhouses within cells that actually produce the brain's energy. Healthy mitochondrial function results in higher levels of ATP—your body's main energy storage molecule—in brain cells.

How does Cognizin enhance focus and concentration?

To sustain your focus and concentration, your brain requires:

1. an adequate ongoing supply of energy and
2. healthy communication between neurons. Not only does Cognizin support healthy brain metabolism, but it also protects your neural structures against free radical damage and provides phospholipids essential to healthy brain function



How does Cognizin-Citicoline improve memory storage and recall?

Cognizin also benefits your brain's ability to recall and remember. Often called a "brain nutrient" because it increases levels of several important neurotransmitters, Cognizin provides important brain nutrients that regulate memory and cognitive function. Cognizin has also been shown to support the activity of nerves that respond to acetylcholine, helping to raise activity levels in the brain's learning and memory circuits.



Cognizin® - Citicoline is easy to use in your products

Manufacturers and formulators will love the more practical benefits of Cognizin. This ingredient is:

- **Pure:** Cognizin contains no food additives, artificial flavors or preservatives.
- **Stable:** Cognizin is stable in liquids and to high heat.
- **Water-soluble:** Cognizin is easy to use in beverages and liquids.
- **Neutral in taste:** Cognizin's neutral and slightly acidic taste compliments numerous product flavours.
- **GRAS:** Cognizin achieved self-affirmed GRAS status in 2009 and is considered safe for food and beverage applications.
- **Vegetarian:** no animal origin material is used in Cognizin.
- **Allergen-free:** Cognizin is considered allergen-free.
- **Kosher:** Cognizin is a certified Kosher ingredient.

The brain is constantly being attacked by various factors of our lifestyle including environmental pollution, internal toxicity, stress and a lack of proper diet and nutrients. Cognizin may help combat the ravages of these effects by stimulating the nervous system process to maintain optimum sustainability of the molecular environment of the brain enabling us to retain our ability to think cognitively and improve our memories.

- Clinical trials have shown Cognizin is effective for combating the effects of certain neurodegenerative processes, thereby allowing for maintenance of optimal memory function.
- Scientific studies have indicated that Cognizin is an effective aid for maintaining normal cognitive function with aging.
- Additional studies point to the ability of Cognizin to act as an antioxidant in preserving normal healthy visual function.
- Cognizin protects neural tissue from the ravages of free radical damage.

Cognizin® - Citicoline product applications

Cognizin is suitable for use in:

-  Dietary supplements
-  Beverages and beverage bases
-  Breakfast cereals
-  Chewing gum
-  Dairy product analogs
-  Frozen dairy desserts
-  Hard and soft candies
-  Milk and milk products
-  Processed fruits and fruits juices

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Did you know?

1. Cognizin Citicoline has three primary health benefits. It helps:

- fuel mental processes
- enhance focus and concentration
- support healthy memory function

2. Cognizin provides the nutrients needed for the body to generate phospholipids. Phospholipids in turn:

- make up approximately 30% of brain tissue
- provide essential protection for neurons
- aid neural communication

3. Cognizin supports brain health across the age spectrum.

Regardless of age, Cognizin Citicoline provides the nutrients needed to support healthy cognition, concentration and memory.

4. Cognizin Citicoline has been clinically studied.

Cognizin has been the subject of several human clinical trials. The recent trial studied the effects of Cognizin on healthy middle-aged adults. Using the latest brain-scanning technology, researchers at the Harvard-associated Brain Imaging Center at McLean Hospital observed increases in brain activity among people who had taken Cognizin for six weeks. Differences were particularly noticeable when participants performed tasks that required sustained attention or memory.

5. Cognizin is safe, vegetarian and allergen-free.

The safety of supplemental Citicoline has been demonstrated in studies in which participants ingested more than the recommended dosage of 250–500 mg per day.

Facts for health professionals

About Cognizin® - Citicoline

Definition

Citicoline is the generic name for synthetic CDP-choline (cytidine diphosphate choline), an organic molecule produced endogenously and found in all living cells. CDP-choline is a precursor for the synthesis of phospholipids that are essential constituents of cell membranes, including phosphatidylcholine, phosphatidylserine, and phosphatidyl-ethanolamine. Because cell membranes have a very high turnover rate, these phospholipids must be continuously synthesized to ensure adequate function of cells.

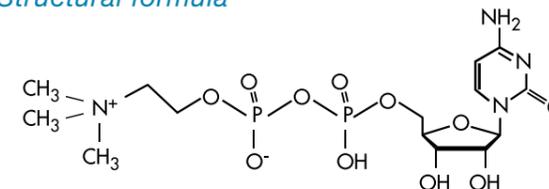
Citicoline is often called a “brain nutrient” because it increases levels of several important neurotransmitters including acetylcholine, dopamine and noradrenaline; helps maintain the integrity of neuronal cell membranes; and increases energy production in the frontal cortex.

The scientific name for citicoline is cytidine 5'-diphosphocholine.

Chemistry

Molecular formula: $C_{14}H_{26}N_4O_{11}P_2$

Structural formula



Sources and metabolism

Diet is not a good source of CDP-choline because the molecule is present in very low amounts in foods. The best sources, liver and brains, are not widely consumed in the United States. Some CDP-choline can be synthesized from dietary choline, which is found in beef, eggs and other foods. Adequate Intake (AI) for choline established by the Food and Nutrition Board of the Institute of Medicine is 550 mg/day for men and 425 mg/day for women.⁽¹⁾ At present there are no nationally representative estimates of intake of either choline or CDP-

choline.

This high-quality brand of pure, stable citicoline is marketed under the brand name Cognizin® citicoline, and is manufactured by Kyowa Hakko Bio Co., Ltd. Citicoline is degraded to uridine and choline during intestinal absorption.⁽²⁾ These two compounds then pass through the blood-brain barrier to reconstitute citicoline in the brain.

Biochemical roles

In the brain, citicoline plays a number of critical roles:

1. Maintains cell integrity through the biosynthesis of structural phospholipids of neuronal membranes

- In animal experiments, supplementation with 500 mg/kg citicoline for 90 days increased the amount of phosphatidylcholine in the frontoparietal cortex by about 30%.⁽⁴⁾
- Citicoline was able to significantly increase phosphatidylcholine, sphingomyelin and cardiolipin levels in gerbils.⁽⁵⁾
- In healthy elderly human subjects, supplementation with 500 mg/day citicoline for 6 weeks was shown by magnetic resonance spectroscopy to stimulate phosphatidylcholine synthesis.⁽⁶⁾

2. Enhances cell signaling by increasing the synthesis of neurotransmitters

- Citicoline administration in laboratory rats produced a rapid increase in acetylcholine production in the dorsal hippocampus and neocortex, as compared to control animals.
- Citicoline increases norepinephrine and dopamine levels in the central nervous system.^(8,9)

3. Increases blood flow and brain metabolism

- Citicoline increased glucose incorporation and metabolism in the brain and increased cerebral blood flow in rats.⁽¹⁰⁾
- Supplementation of human subjects with 500 mg or 2000 mg Cognizin® citicoline for six weeks enhanced frontal lobe bioenergetics with a 14 percent increase in ATP.⁽¹¹⁾
- Citicoline supplementation has been shown

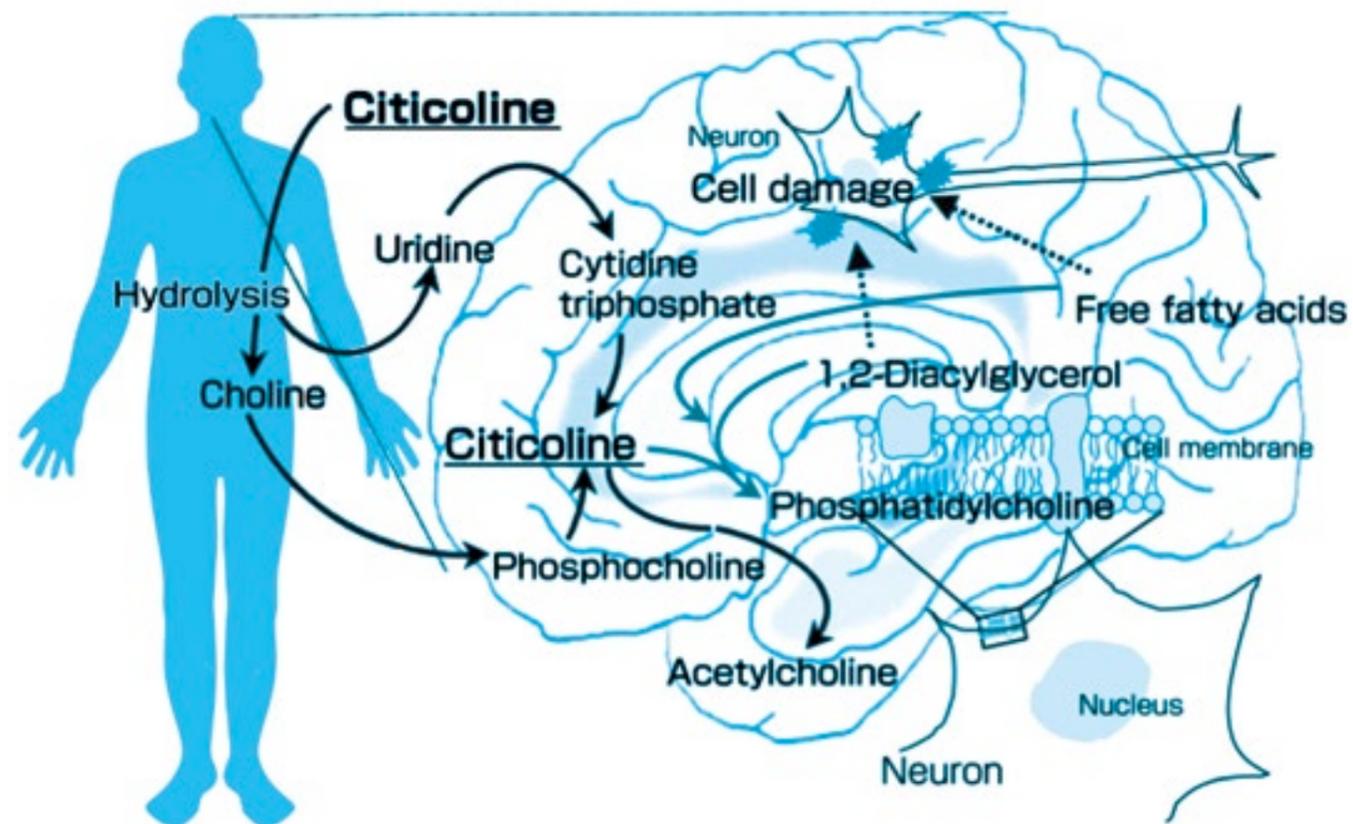
to improve brain metabolism in various animal models of ischemia/reperfusion and to have positive effects on memory and behavior in elderly people.⁽⁸⁾

4. Reduces oxidative stress

- Administration of citicoline has been shown in animal models to help reduce oxidative stress in the brain and promote a normal inflammatory response by inhibiting free fatty acid release, decreasing breakdown of the blood-brain barrier, and attenuating arachidonic acid release.⁽⁵⁾

5. Improved attentional focus

- Healthy, middle-aged women taking 250mg of Cognizin, saw improved attentional focus and inhibition on a test of attention researchers at the Brain Institute at The University of Utah.
- Participants were evaluated with the Continuous Performance Test II (CPT-II), a measure sensitive to attentional function. Results after supplementation showed individuals receiving either the low or high dose of Cognizin citicoline produced fewer commission errors on the CPT-II compared to the placebo group. Specifically, individuals in the two Cognizin citicoline supplemented groups made fewer errors when responding to non-target stimuli.⁽¹⁴⁾



Roles in health

The roles of citicoline in supporting brain structure and function suggest possible benefits in cognitive function in aging. Functional benefits demonstrated in human studies include:

- Supplemental citicoline given to certain groups of elderly people resulted in improvements in measurements of memory,
- attention, behavior, reaction time, relational life, independence and cooperation.⁽⁹⁾
- A meta-analysis of double-blind, randomized human trials on citicoline and cognitive concluded that citicoline modestly
- improves memory and behavioral outcomes.⁽⁸⁾
- Citicoline at a dose of 1,000 mg/day for three months was found to improve verbal memory in a group of healthy older
- adults who were free of any medical, neurological or psychiatric illness but who had relatively inefficient memories.⁽¹²⁾
- In a study of mentally healthy older adults, supplementation with citicoline significantly improved immediate and short
- term memory, suggesting beneficial effects on the underlying cognitive processes of memory retrieval and storage.⁽¹³⁾

Safety

Citicoline has been found to have a very low toxicity profile in toxicology studies in animals and humans. In clinical use it has been observed to be safe at doses up to 2000 mg per day. A drug surveillance study analyzed the results of citicoline treatment in more than 2,800 adults and found minor transient adverse effects in approximately five percent of cases, most commonly stomach pain and diarrhea.⁽⁵⁾

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Kyowa is an international health ingredient manufacturer and a world leader in the development, manufacturing and marketing of nutraceuticals, pharmaceuticals and food products.

Born of Kyowa's dedication to ongoing scientific research, quality management and consumer education, the Cognizin® brand leads the way in clinical brain research.

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