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CHROMIUM

Also Known As:

Acétate de Chrome, Chlorure Chromique, Chlorure de Chrome, Chrome, Chrome III, Chrome 3+, Chrome FTG, Chrome Facteur de Tolérance au Glucose, Chrome Trivalent, Chromic Chloride, Chromium Acetate, Chromium Chloride, Chromium Nicotinate, Chromium Picolinate, Chromium Polynicotinate, Chromium Proteinate, Chromium Trichloride, Chromium Tripicolinate, Chromium III, Chromium III Picolinate, Chromium 3+, Cr III, Cr3+, Cromo, Glucose Tolerance Factor-Cr, GTF, GTF Chromium, GTF-Cr, Kali Bichromicum, Nicotinate de Chrome, Numéro Atomique 24, Picolinate de Chrome, Picolinate de Chrome III, Polynicotinate de Chrome, Potassium Bichromate, Protéinate de Chrome, Trichlorure de Chrome, Tripicolinate de Chrome, Trivalent Chromium.

Scientific Name:

Chromium; Cr; atomic number 24.

People Use This For:

Orally, chromium is used for improving glycemic control in type 1 and 2 diabetes, impaired glucose tolerance (prediabetes), polycystic ovary syndrome (PCOS), corticosteroidinduced hyperglycemia and reactive hypoglycemia, for hypercholesterolemia, and for increasing high-density lipoprotein (HDL) cholesterol levels in patients taking betablockers. It is also used orally for weight loss, to increase muscle mass and fat-free mass, and decrease body fat. Chromium is also used orally to enhance athletic performance, to increase energy and vigor, and to treat dysthymic disorder (a mild form of depression) and atypical depression.

Intravenously, chromium is used as a supplement in total parenteral nutrition (TPN).

Safety:

LIKELY SAFE ... when used orally and appropriately, short-term. Chromium has been safely used in doses up to 1000 mcg/day for up to 6 months (1934, 5039, 5040, 6858, 6859, 6860, 6861, 6862, 6867, 6868) (7135, 7137, 8927, 10309, 13053, 14325, 14440, 17224); however, most of these studies have used chromium doses in a range of 150-600 mcg.

Food and Drug Administration (FDA) and Institute of Medicine (IOM) evaluations of the safety of chromium suggest that it is safe when used in doses of 200 mcg/day for up to 6 months; however, there is insufficient reliable information about the safety of long-term use (13241, 13242).

POSSIBLY SAFE ... when used orally and appropriately, long-term. Chromium has been

safely used in a small number of studies using doses of 200-1000 mcg/day for up to 16 months (7060, 7135, 8927, 11907). Food and Drug Administration (FDA) and Institute of Medicine (IOM) evaluations of the safety of chromium suggest that it is safe when used in doses of 200 mcg/day for up to 6 months; however, there is insufficient reliable information about the safety of long-term use (13241, 13242).

CHILDREN: LIKELY SAFE ...when used orally and appropriately in amounts not exceeding the adequate intake (AI) levels. For infants 0 to 6 months, the AI is 0.2 mcg per day; 7 to 12 months, 5.5 mcg. For children 1 to 3 years, the AI is 11 mcg; 4 to 8 years, 15 mcg. For boys 9 to 13 years, the AI is 25 mcg. For girls 9 to 13 years, the AI is 21 mcg; 14 to 18 years, 24 mcg (7135). There is insufficient reliable information available about the safety of chromium when used in higher amounts in children.

PREGNANCY: LIKELY SAFE ... when used orally and appropriately in amounts not exceeding adequate intake (AI) levels. The AI for pregnant women aged 14 to 18 years is 29 mcg per day. For pregnant women aged 19 to 50 years, it is 30 mcg per day (7135). POSSIBLY SAFE ... when used orally in amounts exceeding the adequate intake (AI) levels. There is some evidence that pregnant patients with gestational diabetes can safely use chromium in doses of 4-8 mcg/kilogram (1953); however, patients should not take chromium supplements during pregnancy without medical supervision.

LACTATION: LIKELY SAFE ...when used orally and appropriately in amounts not exceeding adequate intake (AI) levels. The AI for lactating women aged 14 to 18 years is 44 mcg per day. For lactating women aged 19 to 50 years it is 45 mcg per day (7135). Chromium supplements do not seem to increase normal chromium concentration in human breast milk (1937). There is insufficient reliable information available about the safety of chromium when used in higher amounts in women who are breast-feeding.

Effectiveness:

LIKELY EFFECTIVE

Chromium deficiency. Taking chromium orally is effective for preventing chromium deficiency (7135).

POSSIBLY EFFECTIVE

Diabetes. Some evidence shows that taking chromium picolinate orally can decrease fasting blood glucose, insulin levels, and glycosylated hemoglobin (HbA1C) and increase insulin sensitivity in people with type 2 diabetes (1934, 6867, 7137, 14440). Some evidence also suggests that chromium picolinate might decrease weight gain and fat accumulation in type 2 diabetes patients who are taking a sulfonylurea (14440).

Higher chromium doses might be more effective and work more quickly (6867). Higher doses might also reduce triglyceride and total serum cholesterol levels in some patients (1934, 6867).

Preliminary evidence also suggest that chromium picolinate might have the same benefits in patients with type 1 diabetes (1935) and in patients who have diabetes secondary to corticosteroid use (5039).

Some evidence also shows that a specific combination of biotin and chromium (Diachrome, Nutrition 21) might lower blood glucose levels and HbA1C levels in type 2 diabetes patients who are poorly controlled despite treatment with oral hypoglycemic

agents (12385, 12390, 15169). However, there is no reliable evidence that this combination is more effective than taking chromium alone.

Epidemiological research also links lower toenail chromium levels to increased risk of diabetes and cardiovascular disease, but there is no clinical evidence to suggest that chromium supplements can lower disease risk (11908).

But not all evidence is positive (7060, 8927, 13723, 13731, 14325). An analysis of pooled results from previous studies found inconclusive results due to the small number of trials, small study size, and inconsistent patient populations studied (8927). One of the largest studies that found benefit enrolled patients in China where poor nutritional status is more likely, and therefore, benefit from supplementation is also more likely, compared to Western populations (6867, 14325). There is speculation that chromium supplements might primarily benefit patients with poor nutritional status or low chromium levels. Chromium levels can be below normal in patients with diabetes (7058, 13725).

POSSIBLY INEFFECTIVE

Athletic performance. Taking chromium orally doesn't seem to enhance bodybuilding, strength, or lean body mass. There is some evidence that suggests taking chromium can increase weight loss, body fat loss, and lean body mass in people taking chromium picolinate 200-400 mcg per day in conjunction with resistance training (6860, 6861, 6868). But the results of these studies are unreliable due to questionable methods (6861). More reliable studies show that adding chromium picolinate or chloride 177-200 mcg daily to a weight-training program has no additional beneficial effect on body composition (6861, 6862). Impaired glucose tolerance (Prediabetes). Some evidence suggests that prediabetes patients with impaired glucose tolerance do not have improved glucose tolerance after taking chromium picolinate 400 mcg twice daily for 3 months (13053). Likewise, chromium supplements don't seem to improve glucose tolerance or improve triglyceride or cholesterol levels in elderly patients with impaired glucose tolerance (13722).

INSUFFICIENT RELIABLE EVIDENCE to RATE

Atypical depression. Preliminary clinical research suggests chromium picolinate might help atypical depression (10309).

Beta blocker-induced dyslipidemia. Preliminary research suggests that taking chromium 600 mcg daily for 2 months increases high-density lipoprotein (HDL) levels by 16% in men who take beta-blockers (5040).

Dysthymia. There is some preliminary evidence that chromium might improve the response to antidepressants in people with dysthymic disorder (a mild form of depression). Chromium picolinate or chromium polynicotinate 200 mcg once or twice daily appears to improve mood in patients who have only a partial response to antidepressants such as sertraline or nortriptyline (2659).

Hypoglycemia. Preliminary research suggests that taking chromium chloride 200 mcg daily for 3 months improves symptoms and increase blood glucose levels in patients with reactive hypoglycemia following an oral glucose load (6859).

Myocardial infarction (MI). Epidemiological research suggests that low toenail chromium concentrations are associated with an increased risk of myocardial infarction (13728). However, toenail chromium concentrations might not be a reliable predictor of body stores of chromium. There is also no reliable research showing that chromium supplements can prevent MI.

Obesity. There is conflicting evidence about the effect of chromium on weight loss and obesity. Some clinical research shows that taking chromium picolinate orally might produce modest weight loss of about 1.1 kg compared to placebo when taken over 72-90 days (11962). But other research has found no benefit (6860, 13727, 17224). Two clinical studies show that taking chromium picolinate 400 mcg/day for 12 weeks does not significantly affect body composition, resting metabolic rate, plasma glucose, serum insulin, or serum lipids in overweight military personnel or obese women (6860, 13727). Another preliminary clinical study shows that overweight adults taking 1000 mcg/day do not have significantly reduced body mass index (BMI) or central adiposity compared to placebo after 24 weeks (17224).

Polycystic ovary syndrome (PCOS). Preliminary evidence suggests that chromium picolinate 500 mcg twice daily might increase glucose disposal in women with PCOS (15023).

Turner's syndrome. Preliminary clinical research suggests chromium supplementation might improve abnormalities in glucose and lipid metabolism in patients with Turner's syndrome, a genetic disorder that has a high incidence of diabetes (13729). More evidence is needed to rate chromium for these uses.

Mechanism of Action:

Chromium is an essential trace element. The activity of chromium depends on its valance state. Metallic chromium, or chromium 0, has no activity. The other two common forms, chromium III (Cr III) and chromium VI (Cr VI), have different activities. Cr VI is typically used in chemical and welding industries and is carcinogenic to humans. Cr III is the form found in foods and supplements. Some preliminary research suggests Cr III might be oxidized to Cr VI under physiological conditions (13721).

Chromium is sometimes referred to as glucose tolerance factor (GTF), but GTF is actually a complex of molecules found in the body that includes chromium bound to single molecules of glycine, cysteine, glutamic acid, and two molecules of nicotinic acid. Chromium is thought to be the active component of the complex. Some dietary sources of chromium include canned foods (due to chromium leaching from the can), meats and animal fats, fish, brown sugar, coffee, tea, some spices, calf liver, whole wheat bread, rye bread, and brewer's yeast (7061).

Symptomatic chromium deficiency is rare. When it does occur, it is most often due to malnutrition, pregnancy, stress, or long-term use of chromium deficient total parenteral nutrition (TPN). Symptoms include severe glucose intolerance, weight loss, and metabolic encephalopathy (6863, 13730). Although not yet confirmed, some researchers suspect that tissue levels of chromium might decline with age (6863).

People with diabetes may also have lower chromium levels (7058, 11907, 11908, 13725). Low chromium levels are associated with impaired glucose, insulin, and lipid metabolism, and resultant increased cardiovascular risk (11907). Some athletes might also be at risk for low chromium levels since strenuous aerobic exercise seems to increase urinary excretion of chromium (6860, 6861). However, exercise-induced losses seem to be less in those who regularly exercise (6862). People who strength train seem to have increased absorption of chromium (7136). It is difficult to measure chromium status to determine who might require supplementation. Blood chromium levels are not in equilibrium with chromium stores and, therefore, do not provide a good indicator of chromium status (6859). However, elevated

blood chromium levels may indicate excessive chromium exposure (11786). Levels in the urine and hair do not reflect overall chromium status (6867). There is no reliable method available to diagnose chromium deficiency, other than observing the outcome following supplementation in patients suspected of being deficient (3859, 6869). Symptoms of chromium deficiency can include impaired insulin function and glucose tolerance, increased serum cholesterol and triglycerides, neuropathy, weight loss, decreased respiratory function, and nitrogen metabolism abnormalities (6863, 6869, 11786).

Discovery of the role of chromium in insulin function occurred when patients on long-term TPN developed symptoms of diabetes that did not respond to insulin, but were reversed by chromium (6869). Because of the symptoms associated with chromium deficiency, researchers have speculated that chromium supplementation might be an effective treatment for diabetes and hypercholesterolemia. There is some evidence that patients with diabetes might have lower than normal levels of chromium due to increased chromium excretion (6858). However, patients with diabetes also seem to have increased gastrointestinal absorption of chromium. It's also theorized that patients with diabetes may not be able to adequately convert chromium from the diet to a usable form in the body (6867). Chromium seems to be transported to insulin-sensitive cells by transferrin, in response to increases in plasma insulin levels (6869). It is suspected to potentiate insulin by increasing receptor numbers and affinity, and increasing insulin binding to cells (6859, 6867). A single oral dose of chromium before a high carbohydrate meal seems to lessen postprandial hyperglycemia in healthy, young volunteers. This suggests chromium potentiates the effect of insulin (13726).

In animal models, a chromium-containing peptide called chromodulin has been identified, which potentiates the actions of insulin at its receptors, including activation of receptor tyrosine kinase activity (6869). In patients with diabetes, these actions seem to translate into decreased insulin resistance, improved glucose tolerance, and lower blood glucose levels (6862). Researchers are interested in chromium for treatment of obesity and metabolic syndrome (syndrome X) due to its potential effects on lipids and body composition. Some clinical research suggests that chromium might reduce oxidative stress, and thereby some of the adverse effects of diabetes, in patients with poorly controlled diabetes. In patients without diabetes, chromium might act as a pro-oxidant (13724). But the clinical significance of this is not known.

Some research suggests that chromium might also sensitize insulin-sensitive glucoreceptors in the brain, resulting in appetite suppression, activation of the sympathetic nervous system, stimulation of thermogenesis, and down-regulation of insulin secretion (6170, 6860). It is also theorized that chromium might enhance glucose utilization in the brain and stimulate norepinephrine release (2659). Preliminary clinical research suggests that chromium decreases endocrine responses to serotonin receptor stimulation, which could produce antidepressant activity (8929). Chromium is also hypothesized to increase muscle mass by increasing amino acid uptake into muscle cells via potentiation of insulin activity (6862). Chromium supplements come in several salt forms. The most common are chromium picolinate, chromium nicotinate, chromium and picolinic acid, which is a naturally occurring metabolic derivative of tryptophan.

Chromium polynicotinate is often referred to as niacin bound chromium because it includes

chromium bound to molecules of niacin.

Adding the picolinate or nicotinate salt increases absorption, retention, and accumulation of chromium compared to inorganic salts such as chromium chloride (6861, 6864, 9141). Some manufacturers suggest that chromium polynicotinate is better absorbed that chromium picolinate. But there is not scientific support for this.

When ingested, most chromium is excreted unabsorbed in the feces. The small percentage that is absorbed, typically 0.4% to 2.5%, is rapidly excreted in the urine (7135). Once absorbed, chromium concentrates in the kidney, heart, liver, brain, muscle, spleen, testes, epididymis, and lungs (6863).

Chromium picolinate seems to be handled differently in the body than dietary chromium (6869). There is some evidence that chromium picolinate can enter cells unchanged and then produce hydroxyl radicals when the chromium is released, which might cause DNA damage (1299, 6869). This may be due to its higher solubility and lipophilicity compared with other chromium compounds (11786). The clinical significance of this potential harmful effect is not known.

Adverse Reactions:

Orally, chromium in the trivalent form (Cr III) is generally well tolerated. However, some patients can experience cognitive, perceptual, and motor dysfunction at doses as low as 200-400 mcg per day of chromium picolinate (1935). Chromium picolinate has also been associated with weight gain in young women who do not exercise and in those on a weight-lifting program (1938). Some patients can also experience headaches, insomnia, sleep disturbances, irritability, and mood changes (6860). Acute chromium toxicity can cause vomiting, diarrhea, hemorrhage, and blood loss into the gastrointestinal tract resulting in cardiogenic shock (11786).

Chronic use of chromium picolinate in higher doses might cause significant adverse effects. Some reports have linked chromium in doses of 600-2400 mcg/day with anemia, thrombocytopenia, hemolysis, hepatic dysfunction, or renal failure in some patients (554); however, it is not clear if chromium is the cause of these adverse effects.

Chromium picolinate has been associated with at least one report of chronic interstitial nephritis and two reports of acute tubular necrosis (554, 1951, 14312). Laboratory evidence suggests that chromium does not seem to cause kidney tissue damage even after long-term, high-dose exposure (7135); however, patient- or product-specific factors could potentially increase the risk of chromium-related kidney damage. More evidence is needed to determine what role, if any, chromium has in potentially causing kidney damage. Acute hepatitis has been reported in a patient taking chromium polynicotinate 200 mcg daily for 5 months (9141). Symptoms resolved when the product was discontinued. Two other cases of hepatotoxicity have been reported in patients who took a specific combination product (Hydroxycut) which also contained chromium polynicotinate in addition to several herbs (13037).

A specific combination product (Hydroxycut) containing chromium, caffeine, and ephedra has been associated with seizures (10307). But the most likely causative agent in this case is ephedra.

Hexavalent chromium (CR VI) is 100 times more toxic than trivalent chromium. It can cause hepatic, renal, and cardiac failure (9141). Occupational inhalation of hexavalent

chromium can cause ulceration of the nasal mucosa and perforation of the nasal septum, and has been associated with pneumoconiosis, allergic asthma, and increased susceptibility to respiratory tract carcinomas. Industrial hexavalent chromium is considered cytotoxic and genotoxic (6863). It penetrates the cells easily (unlike trivalent chromium) and appears to induce oxidative damage to DNA (7326).

Some preliminary research suggests trivalent chromium might be oxidized to hexavalent chromium in the body (13721). Other research suggests that in euglycemic patients chromium might act as a pro-oxidant (13724). These concerns have caused some researchers to question the safety of chromium supplementation (13721); however, the clinical significance of these findings is not known.

Intravenously, chromium is associated with decreased glomerular filtration rate (GFR) in children who receive long-term chromium-containing total parenteral nutrition - TPN (11787).

Interactions with Herbs & Supplements:

CHROMIUM-CONTAINING HERBS AND SUPPLEMENTS: Herbs that contain chromium can increase the risk of chromium toxicity when taken chronically, or when taken with chromium supplements (9141). Some chromium-containing herbs include bilberry, brewer's yeast, cascara, and horsetail.

IRON: Chromium competes with iron for binding to the transport protein, transferrin, and could predispose people to iron deficiency. This effect is unlikely to be clinically significant at usual supplemental doses of chromium (6861, 6865, 6866).

VITAMIN C: Concomitant vitamin C use might increase chromium absorption (7135). **ZINC**: Theoretically, co-administration might decrease absorption of both chromium and zinc (1950).

Interactions with Drugs:

INSULIN

Interaction Rating = **Moderate** Be cautious with this combination. Severity = Moderate • Occurrence = Possible • Level of Evidence = D

Theoretically, concomitant use might increase the risk of hypoglycemia (1952).

LEVOTHYROXINE (Synthroid, Levothroid, Levoxyl, and others)

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Probable • Level of Evidence = B

Clinical research in healthy volunteers shows that taking chromium picolinate 1000 mcg with levothyroxine 1 mg decreases serum levels of levothyroxine by 17% compared to taking levothyroxine alone. It is thought that chromium might bind levothyroxine in the intestinal tract and decrease levothyroxine absorption (16012). Advise patients to take levothyroxine at least 30 minutes before or 3-4 hours after taking chromium.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) Interaction Rating = Minor Be watchful with this combination.

Severity = Mild • Occurrence = Possible • Level of Evidence = D

There is some evidence that NSAIDs might increase chromium levels by increasing chromium absorption and retention. Drugs that are prostaglandin inhibitors seem to increase chromium absorption and retention (7135). Some of these drugs include ibuprofen (Advil, Motrin, Nuprin, others), indomethacin (Indocin), naproxen (Aleve, Anaprox, Naprelan, Naprosyn), piroxicam (Feldene), aspirin, and others.

Drug Influences on Nutrient Levels and Depletion:

ANTACIDS: There is some evidence that antacids might decrease chromium levels by inhibiting absorption of chromium, but the clinical significance of this isn't clear. Increasing gastric pH seems to decrease chromium absorption due to formation of less soluble chromium salts (7135).

CORTICOSTEROIDS: Use of corticosteroids can increase urinary chromium excretion, which might lead to chromium deficiency and/or corticosteroid-induced hyperglycemia (5039).

H2-BLOCKERS: There is some evidence that H2-blockers might decrease chromium levels by inhibiting absorption of chromium, but the clinical significance of this isn't clear. Increasing gastric pH seems to decrease chromium absorption due to formation of less soluble chromium salts (7135). The H2 blockers include cimetidine (Tagamet), ranitidine (Zantac), nizatidine (Axid), and famotidine (Pepcid).

PROTON PUMP INHIBITORS (PPIs): There is some evidence that PPIs might decrease chromium levels by inhibiting chromium absorption, but the clinical significance of this isn't clear. Increasing gastric pH might decrease chromium absorption due to formation of less soluble chromium salts (7135). PPIs include omeprazole (Prilosec), lansoprazole (Prevacid), rabeprazole (Aciphex), pantoprazole (Protonix, Pantoloc), and esomeprazole (Nexium).

Interactions with Foods:

None known.

Interactions with Lab Tests:

None known.

Interactions with Diseases or Conditions:

BEHAVIORAL AND PSYCHIATRIC DISORDERS: Theoretically, chromium picolinate preparations might affect behavioral and psychiatric conditions. Picolinic acid in chromium picolinate preparations can alter serotonin, dopamine, and norepinephrine metabolism in the central nervous system (1935).

CHROMATE/LEATHER CONTACT ALLERGY: Oral chromium supplements can cause allergic reactions in people with chromate or leather contact allergy, including dermatitis, erythema, and scaling on the extremities (6624).

DIABETES: Chromium might lower blood glucose levels (1939). Theoretically, chromium might increase the risk of hypoglycemia if used with other diabetes drugs. Tell patients with diabetes to use chromium products cautiously and monitor blood glucose levels closely. Dose adjustments to diabetes medications might be necessary.

LIVER DISEASE: The chromium polynicotinate form of chromium has been linked to hepatotoxicity in at least three cases (9141, 13037). Theoretically, taking chromium polynicotinate might exacerbate symptoms in patients with existing liver disease. Advise these patients to avoid chromium polynicotinate supplements.

RENAL DISEASE: There are at least three reports of kidney damage in patients who took chromium picolinate (554, 1951, 14312). Theoretically, chromium might exacerbate renal disease. Advise patients with renal dysfunction to avoid chromium supplements.

Dosage/Administration:

ORAL: For type 2 diabetes, 200-1000 mcg daily in divided dose has been used (1934, 6867, 7137, 8927, 14440). A specific combination product providing chromium 600 mcg plus biotin 2 mg daily (Diachrome, Nutrition 21) has also been used (15169).

For dyslipidemia in men taking beta-blockers, 200 mcg three times daily has been used (5040).

For corticosteroid-induced hyperglycemia or exacerbation of pre-existing diabetes, 400 mcg per day or 200 mcg three times daily has been used (5039).

For preventing reactive hypoglycemia, 200 mcg daily of chromium chloride has been used (6859).

For treating dysthymic disorder (mild depression), 200 mcg once or twice daily of chromium picolinate or polynicotinate has been used (2659).

For polycystic ovary syndrome (PCOS), chromium picolinate 500 mcg twice daily has been used (15023).

Chromium picolinate has been used in most studies.

There is insufficient information to establish safe and tolerable upper intake levels of chromium (7135); however, daily adequate intake (AI) levels for chromium have been established: Infants 0 to 6 months, 0.2 mcg; 7 to 12 months, 5.5 mcg; children 1 to 3 years, 11 mcg; 4 to 8 years, 15 mcg; boys 9 to 13 years, 25 mcg; men 14 to 50 years, 35 mcg; men 51 and older, 30 mcg; girls 9 to 13 years, 21 mcg; 14 to 18 years, 24 mcg; women 19 to 50 years, 25 mcg; women 51 and older, 20 mcg; pregnant women 14 to 18 years, 29 mcg; 19 to 50 years, 30 mcg; lactating women 14 to 18 years, 44 mcg; 19 to 50 years, 45 mcg. Sometimes chromium amounts are listed in micromols. The conversion factor to micrograms is: 1.92 micromol Cr = 100 mcg (6867).

INTRAVENOUS: No typical dosage.

Editor's Comments:

Chromium was discovered in France in the late 1790s, but it took until the 1960s before it was recognized as being an important trace element and important for insulin function (7058).

This monograph was last reviewed on 12/17/2012 and last updated on 08/11/2011. Monographs are reviewed and/or updated multiple times per month and at least once per year. If you have comments or suggestions on something that should be reviewed or included, please tell the editors. For details about our evidence-based approach, see our Editorial Principles and Process.

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