

CAS#: 10034-81-8, 7778-74-7, 7790-98-9, 7601-89-0, 7791-03-9

Division of Toxicology and Environmental Medicine

September 2008

This Public Health Statement is the summary chapter from the Toxicological Profile for Perchlorates. It is one in a series of Public Health Statements about hazardous substances and their health effects. A shorter version, the ToxFAQsTM, is also available. This information is important because these substances may harm you. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present. For more information, call the ATSDR Information Center at 1-800-232-4636.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites are then placed on the National Priorities List (NPL) and are targeted for long-term federal clean-up activities. Perchlorates have been found in at least 49 of the 1.581 current or former NPL sites. The possibility exists that the number of sites at which perchlorates are found may increase in the future as more sites are evaluated. In addition, perchlorate exposure has been found to be more widespread, so that waste sites are only a part of the potential perchlorate sources. Other potential sources of exposure include food, some water supplies, fireworks, road flares, consumer products such as bleach and matches, and natural sources.

When a substance is released either from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. Such a release does not always lead to exposure. You can be exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance, or by skin contact

If you are exposed to perchlorates, many factors will determine whether or not you will be affected. These factors include the physical form of the chemical, the dose (how much), the duration (how long), and how you come in contact with them. You must also consider any other chemicals to which you are exposed and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT ARE PERCHLORATES?

The terms perchlorate or perchlorate anion refer to a negatively charged group of atoms consisting of a central chlorine atom bonded to four oxygen atoms. Perchlorate has the molecular formula ClO_4^- . The terms perchlorates or perchlorate salts refer to the inorganic compounds that contain the perchlorate anion bonded to a positively charged group such as ammonium or an alkali or alkaline earth metal.

Perchlorates can form naturally in the atmosphere, leading to trace levels of perchlorate in precipitation. High levels of perchlorates occur naturally in some locations, such as regions of west Texas and northern Chile.

Perchlorates are colorless and have no odor. Five perchlorates are manufactured in large amounts: magnesium perchlorate, potassium perchlorate, ammonium perchlorate, sodium perchlorate, and lithium perchlorate. Perchlorates are found in the environment in two forms, either as a solid or dissolved in water. If no water is present, as in a drum or on top of dry ground, then they will exist as solids. If water is present, then they will quickly dissolve. When perchlorates dissolve, they separate into two parts. One part has a positive charge, and

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the other part has a negative charge. The part with the negative charge is called the perchlorate anion or just perchlorate. This is the part of the chemical that people look for in the environment or in your body.

Perchlorates are stable at normal temperatures, but when they are heated to a high temperature, they begin to react. Once they begin to react, they produce a large amount of heat. This causes more of the perchlorates to begin reacting, which makes even more heat. This chain reaction process repeats itself over and over until an explosion occurs. Because perchlorates react this way, they are used in rocket motors, fireworks, flares, gunpowder, and explosives.

Because perchlorates can react quickly at high temperatures, people did not expect to find them in the environment. But at normal Earth temperatures, perchlorates react much more slowly. We have learned only recently that perchlorates may last in the environment unreacted for several years.

One of the perchlorate salts, ammonium perchlorate, is produced in large amounts because it is used in rocket fuels. The solid booster rocket on the space shuttle is almost 70% ammonium perchlorate. Perchlorates are also used in explosives. Because perchlorates are used for some military applications, many countries consider the amounts that they make confidential. This is one reason why we do not know the exact amount of perchlorates produced or used in the United States or around the world. As with most chemicals, private companies in the United States are not required to provide information on the amount of perchlorates that they make or use. We also do not know the exact amount of perchlorates brought into the United States from other countries, although the largest amount probably comes from fireworks. It is important to note that production figures for a limited set of the larger profile of perchlorate applications do not readily translate into environmental release data or accurately characterize the universe of perchlorate uses and potential for release.

Other uses of perchlorates include temporary adhesives, electrolysis baths, batteries, air bags, drying agents, etching agents, cleaning agents and bleach, and oxygen generating systems. Little data are available on the nature, amount, and potential for release of these possible sources of perchlorate to the environment. Perchlorates are also used for making other chemicals. Many years ago, perchlorates were used as a medication in the United States to treat overactive thyroid glands, and they still have some medical uses in the United States and other parts of the world. Perchlorate is also used in treatment of side effects of amiodarone, a drug used in the treatment of cardiac arrhythmias and angina.

1.2 WHAT HAPPENS TO PERCHLORATES WHEN THEY ENTER THE ENVIRONMENT?

Perchlorates are soluble in water and generally have high mobility in soils. This characteristic results in their ability to move from soil surfaces into groundwater (a process called leaching) when they enter the environment. Perchlorates are ionic substances and therefore, do not volatilize from water or soil surfaces. Perchlorates are known to remain unreacted in the environment for long



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periods of time; however, there is evidence that microorganisms found in soil and water may eventually reduce perchlorate to other substances. If perchlorates are released to air, then they will eventually settle out of the air, primarily in rainfall. Perchlorates do not appear to accumulate in animals. Our understanding of perchlorates continues to evolve, and scientific understanding related to perchlorates will continue to be reviewed and re-evaluated when new information becomes available

Before 1997, it was very hard to measure perchlorates in the environment. In 1997, a much better method was developed, and low levels of perchlorates in water and other media can now be measured. Scientists first began looking for perchlorates near sites where they had been used or discarded, and were surprised when they found them in many other places, including areas where there was no known perchlorate use. They did not think that perchlorates would last very long in the environment because of perchlorate's reactivity. Since then, scientists have been looking for perchlorates in water at more and more places. Perchlorates have recently been found in environmental media such as soil, plants, and animals located in areas where perchlorate was used and released, and in areas where there was no known use or man made releases of perchlorates.

Perchlorates can enter the environment from several sources, both human-made (called anthropogenic) and natural sources. Since perchlorate is used in rockets and certain military applications, the manufacture, use, and disposal of products like rockets and missiles has led to perchlorate being released into the environment. When rockets undergo successful launches, the intense heat leads

to nearly complete reaction of the perchlorate. Therefore, release of perchlorate to the environment often occurs when its intended use does not occur (for example, dismantling and disposal of rockets, accidental release from manufacturing facilities, or unsuccessful rocket launches). In the past, some of these activities resulted in high levels of perchlorate contamination of soil and groundwater at many military installations and rocket manufacturing facilities. Today, great effort is made to minimize the release of perchlorates when rockets or missiles are dismantled or when perchlorates are manufactured. Other human-made sources for perchlorate release into the environment include road-side safety flares and fireworks. Perchlorate has also been detected at low levels as an impurity in certain consumer products such as bleach, and the use and disposal of these products could also lead to releases. Perchlorate is a natural component of a nitrate fertilizer from Chile that was imported and regularly used in the United States for many years. Although the use of this fertilizer has declined in recent years, perchlorate was released directly to soil and plants in areas where this fertilizer was applied. In addition, there appear to be natural sources of perchlorate in the environment. Perchlorates can form naturally in the atmosphere, leading to trace levels of perchlorate in rainfall. Higher than expected levels of perchlorates occur naturally in some locations such as regions of west Texas, New Mexico, and northern Chile. A combination of human activities and natural sources. has led to the widespread presence of perchlorates in the environment



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1.3 HOW MIGHT I BE EXPOSED TO PERCHLORATES?

You may be exposed to perchlorates if you eat food or drink water that contains perchlorates. Perchlorates have been found in food and milk. Some plants, especially leafy green vegetables, have been found to have elevated levels of perchlorate. When water containing perchlorate is used to irrigate the plants, perchlorate is left behind when water evaporates from the leaves of the plants. Cows may eat fodder containing perchlorate and pass them on in their milk. The Food and Drug Administration (FDA) recently published the results of measurements of perchlorate and iodine levels in the food supply. The FDA found that 74% of the foods analyzed had at least one sample in which perchlorate was detected. The perchlorate dietary intake was estimated for 14 different age/gender groups in the United States. The lowest intake range was estimated as 0.08-0.11 µg/kg/day (micrograms/kilogram/day) for males aged 25-30 years, and the highest estimated intake was to be 0.35–0.39 µg/kg/day for children 2 years old. These levels are not expected to affect human health. The FDA did not recommend any changes in eating habits of Americans based upon the measured levels of perchlorate.

Perchlorates have been found in lakes, rivers, and groundwater wells. Perchlorate has been identified at least once in approximately 4% of over 3,800 community water systems sampled throughout the United States. From 26 different states and 2 territories, the detectable levels averaged 9.8 μ g/L (micrograms/liter) and ranged from the minimum reporting level of 4 μ g/L to a maximum at 420 μ g/L.

Additional potential sources of perchorate may be found if you live near a rocket manufacturing or testing facility, if you live near or work at a factory where they are made, or if you live near a factory that makes fireworks, flares, or other explosive devices. As mentioned earlier, perchlorate is being found in small amounts in areas where it has not been known to be manufactured, used, or released by humans. Exposure to perchlorates at these locations may be possible because natural levels of perchlorates occur in the environment.

Perchlorate has been detected at low levels as an impurity in certain products that are commonly used by humans. Some of these products include bleach and cleaning products that may contain bleach, bottled water, and tobacco products; even some nutritional supplements (vitamins and minerals) have been found to contain perchlorates. However, vitamin and mineral supplements are typically formulated to include iodine, a factor that would provide protection against any possible effect of perchlorate.

1.4 HOW CAN PERCHLORATES ENTER AND LEAVE MY BODY?

Perchlorates can enter the body after you have swallowed food or water containing them. Since they easily dissolve in water, they quickly pass through the stomach and intestines and enter the bloodstream. If you breathe in air containing dust or droplets of perchlorate, it can pass though your lungs and enter the bloodstream. Perchlorates probably do not enter the body directly through the

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skin, but if present on your hands, hand-to-mouthactivity could contribute to oral exposure.

The blood stream carries perchlorate to all parts of the body. Perchlorate is not changed inside the body. A few internal organs (for example, the thyroid, breast tissue, and salivary glands) can take up relatively large amounts of perchlorate from the bloodstream. Perchlorate generally leaves these organs in a few hours.

When perchlorates are swallowed, a small percentage is eliminated in the feces. More than 90% of perchlorate taken in by mouth enters the bloodstream. In the blood, perchlorate passes into the kidneys, which then release it into the urine. The body begins to clear itself of perchlorate through the kidneys within 10 minutes of exposure. Although most of the perchlorate that is taken into the body is quickly eliminated, the presence of perchlorate in many foods and in some drinking water sources means that exposure may continue to occur on a daily basis.

1.5 HOW CAN PERCHLORATES AFFECT MY HEALTH?

The main target organ for perchlorate toxicity in humans is the thyroid gland. Perchlorate has been shown to partially inhibit the thyroid's uptake of iodine. Iodine is required as a building block for the synthesis of thyroid hormone. Thyroid hormones regulate certain body functions after they are released into the blood. Although not demonstrated in humans, it is anticipated that people exposed to excessive amounts of perchlorate for a long time may develop a decreased production

of thyroid hormones. The medical name for this condition is hypothyroidism. Hypothyroidism is usually caused by conditions totally unrelated to perchlorates. In hypothyroidism, the lower amounts of thyroid hormones in your blood cause increases in pituitary hormones that can lead to an increase in the size of the thyroid gland. The medical name for this condition is goiter. Because thyroid hormones perform important functions throughout the body, many normal body activities also are affected by the lower hormone levels. Because perchlorates were known to lower thyroid hormone levels, at one time, perchlorates were given as a drug (more than 400 mg per day, which is many times higher than the doses that people receive from environmental exposures) to treat people with overactive thyroid glands (a condition known as hyperthyroidism). Side effects seen in a small number of treated patients were skin rashes, nausea, and vomiting. A few patients developed severe shortages of blood cells, and some of them died. Healthy volunteers who took approximately 35 mg of perchlorate every day (equivalent to drinking 2 liters of water containing 17 mg/L or 17 parts per million [ppm] perchlorate every day) for 2 weeks or 3 mg daily for 6 months (equivalent to drinking 2 liters of water containing 1.5 mg/L [1.5 ppm] perchlorate every day) showed no signs of abnormal functioning of their thyroid gland. A study of adults in Nevada found that the number of cases of thyroid disease in a group of people who drank water contaminated with perchlorate was no different than the number of cases found in a group of people who drank water without perchlorate. This means that levels of perchlorate in the water were not the cause of the thyroid disease, and a search of the literature confirms no evidence of perchlorate inducing thyroid disease. Two studies of people who worked for years in the production of perchlorate found no



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evidence of alterations in the workers' thyroids, livers, kidneys, or blood. One of these studies estimated that the workers may have taken up about 34 mg of perchlorate per day. A recent study showed that perchlorate levels to which the general population of the United States is exposed via food and drinking water, were associated with changes in thyroid hormone levels in women with low iodine intake, suggesting that the effect of perchlorate in people depends on gender, the length of exposure, and how much iodine the people consume. Further research is recommended to affirm these findings.

As mentioned in the preceding sections, perchlorate is a naturally occurring chemical that has been found in some foods and in some drinking water supplies. Other naturally occuring chemicals, such as thiocyanate (in food and cigarette smoke) and nitrate (in some food), are also known to inhibit iodide uptake. Further studies are needed to completely answer all questions about potential toxicity of perchlorate.

The thyroid gland is also the main target organ for perchlorate toxicity in animals. The thyroid changes caused by perchlorate in animals may lead to tumors in the thyroid after a long period. This has occurred after administering high amounts (928 to 2,573 milligrams perchlorate/kg/day) of perchlorate to the animals. The National Academy of Sciences (NAS) concluded that based on the understanding of the biology of human and rodent thyroid tumors, it is unlikely that perchlorate poses a risk of thyroid cancer in humans. Perchlorates have not been classified for carcinogenic effects by the Department of Health and Human Services (DHHS) or the International Agency for Research on Cancer (IARC). The EPA has determined that perchlorate is not likely to pose a risk of thyroid

cancer in humans, at least at doses below those necessary to alter thyroid hormone homeostasis, based on the hormonally-mediated mode of action in rodent studies and species differences in thyroid function

Studies in animals also showed that perchlorate did not affect the reproductive organs or the animals' capacity to reproduce. The NAS found that the studies in animals provided important information, but their usefulness to predict whether harmful effects could occur in humans is small

1.6 HOW CAN PERCHLORATES AFFECT CHILDREN?

This section discusses potential health effects in humans from exposures during the period from conception to maturity at 18 years of age.

Children and developing fetuses may be more likely to be affected by perchlorate than adults because thyroid hormones are essential for normal growth and development. Two studies were conducted of newborn babies and school-age children from an area in Chile where levels of perchlorate in the drinking water were much higher than those detected in some U.S. water supplies due to natural sources of perchlorate. No evidence of abnormal thyroid function was found among the babies or the children. The mothers and the children may have taken approximately 0.2 mg of perchlorate per day in the drinking water. Some studies of newborn babies in areas from Arizona, California, and Nevada, where perchlorate has been found in the drinking water, have not provided convincing evidence of thyroid abnormalities associated with

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perchlorate. A Centers for Disease Control and Prevention (CDC) study of people all over the United States showed that all of the people that were tested had detectable concentrations of perchlorate in their urine, thus making it difficult to find an unexposed comparison group as a control population.

As indicated above, perchlorate has been found in breast milk, so that nursing mothers can transfer perchlorate to their babies. Nevertheless, the beneficial aspects (biological and psychological) of breast-feeding outweigh any risks from exposure to perchlorate from mother's milk, especially if they consume adequate iodine from food and supplements.

Animal studies have shown a low level of thyroid activity in developing animals exposed to perchlorates through the placenta before birth or through the mother's milk after birth. Modern studies of the effects of perchlorate on developing animals have been conducted mostly in rats. Several studies in which pregnant rats were given relatively low amounts of perchlorate have shown that perchlorate can alter the thyroid gland in the newborn animals. This has generally occurred when perchlorate also affected the thyroid of the mothers. In addition, a study suggested an alteration in an area of the brain of pups born to rats. The NAS (2005) indicated that rats are more sensitive to agents that disturb thyroid function than are humans, so the relevance of rat studies in quantitative terms to humans is limited.

1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO PERCHLORATES?

Although perchlorate is present in food, milk, and drinking water, it is very unlikely that it will be present in the air of the average home or apartment. Perchlorates are found in some consumer products that people use. They are present in highway and marine signal flares, small fireworks, gunpowder, and matches. Storing these items out of the reach of children and not igniting them in a closed environment, such as inside the house or the garage, will decrease the potential for exposure.

Although perchlorate has been detected in a few samples of bottled water, the levels have been very low. Therefore, if you live near a location where perchlorates have been found in drinking water at high levels, using bottled drinking water may reduce the risk to your family, particularly if you drink well water that may contain perchlorate. If you live in one of these areas, prevent your children from playing in dirt and from eating dirt. Make sure your children wash their hands frequently, and before eating. Discourage your children from putting their hands in their mouths or doing other hand-to-mouth activities. You may also contact local public health authorities and follow their advice.

If you work in a factory that makes or uses perchlorates, it is possible to carry perchlorate dust from work on your clothing, skin, or hair. You may then get perchlorate dust in your car, home, or other locations outside of work where family members might be exposed. You should know about this possibility if you work with perchlorates. Taking a

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shower will remove any perchlorate dust from your skin or hair. Washing your clothes will remove any perchlorates dust from them.

1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN **EXPOSED TO PERCHLORATES?**

Methods to measure perchlorate in the body are not routinely available, but perchlorate can be measured in the urine. Because perchlorate leaves the body fairly rapidly (in a matter of hours), perchlorate in the urine can only indicate very recent exposure. Levels of thyroid hormones in the blood can be monitored. Such tests will tell you if your hormone levels are altered, but will not tell you the cause (exposure to perchlorate is only one of many possibilities). Medical tests can also measure the capacity of the thyroid gland to take iodide from the blood to manufacture thyroid hormones. Exposure to perchlorate can decrease this capacity, but so can exposure to other chemicals, as well as iodine deficiency and medical conditions unrelated to any exposure to chemicals.

1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government develops regulations and recommendations to protect public health. Regulations *can* be enforced by law. The EPA, the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA) are some federal agencies that develop regulations for toxic substances. Recommendations provide valuable guidelines to protect public health, but *cannot* be enforced by law. The Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH) are two federal organizations that develop recommendations for toxic substances.

Regulations and recommendations can be expressed as "not-to-exceed" levels, that is, levels of a toxic substance in air, water, soil, or food that do not exceed a critical value that is usually based on levels that affect animals; they are then adjusted to levels that will help protect humans. Sometimes these not-to-exceed levels differ among federal organizations because they used different exposure times (an 8-hour workday or a 24-hour day), different animal studies, or other factors.

Recommendations and regulations are also updated periodically as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for perchlorates include the following:

The EPA is currently undertaking efforts to make a determination as to whether or not a national primary drinking water regulation is needed for perchlorate. To make this determination, EPA is evaluating information to more fully characterize perchlorate exposure to determine if regulation of perchlorate in drinking water would represent a meaningful opportunity for reducing risks to human health as required under the Safe Drinking Water Act (SDWA).

The EPA has developed a Reference Dose (RfD) of 0.0007 mg/kg/day for perchlorate. The RfD is an estimate of a daily oral exposure to the human

DEPARTMENT of HEALTH AND HUMAN SERVICES, Public Health Service Agency for Toxic Substances and Disease Registry

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population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime. This RfD leads to a drinking water equivalent level (DWEL) of 24.5 ppb. EPA calculates the DWEL using the RfD, multiplied by an adult body weight of 70 kg, and divided by a tap water consumption value of 2 L/day. EPA's Office of Solid Waste and Emergency Response has provided guidance for perchlorate that indicates that the RfD and its corresponding DWEL of 24.5 ppb are respectively the recommended "to be considered" (TBC) value and the preliminary remediation goal (PRG) for cleanup under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA). The EPA is also responsible for developing guidelines for controlling hazardous waste from the time it is generated until its ultimate disposal-in effect, from "cradle to grave".

The Department of Transportation (DOT) has designated perchlorate as a hazardous material and limits the quantity that is transported aboard aircraft and vessels. The DOT also provides identification and protective guidance for an emergency response to a transportation incident involving a hazardous material.

The Department of Defense (DOD) must comply with any EPA cleanup standards and processes under all applicable environmental laws and regulations, including CERCLA, the Resource Conservation and Recovery Act (RCRA), the Clean Water Act (CWA), and the SDWA. DOD policy requires the testing of perchlorate when it is reasonably expected that a release has occurred. Specifically, the DOD's policy states that in the absence of federal or state standards, if perchlorate levels in water exceed 24 ppb (current level of

concern for managing perchlorate), a site-specific risk assessment must be conducted. When an assessment indicates that the perchlorate contamination could result in adverse health effects. the site must be prioritized for risk management. DOD will also comply with applicable state or federal promulgated standards, whichever is more stringent. Additionally, DOD established the Emerging Contaminants Directorate in 2006 to help the department proactively approach emerging contaminants to enable a fully informed, risk-based investment decision process that protects human health and DOD operations capabilities; perchlorate is one of seven emerging contaminants included on DOD's Action List

The FDA has developed Dietary Guidelines that promote health and reduce risk for chronic diseases through diet and physical activity. FDA is not recommending any changes to infants' and children's diets and eating habits based on current perchlorate data. FDA continues to recommend a healthy eating plan, consistent with the Dietary Guidelines for Americans, that emphasizes fruits, vegetables, whole grains, and fat-free or low-fat milk and milk products; includes lean meats, poultry, fish, beans, eggs, and nuts; and is low in saturated fats, trans fats, cholesterol, salt (sodium), and added sugars. Additionally, adequate intake of iodine has previously been recognized as important for healthy thyroid function.

1.10 WHERE CAN I GET MORE **INFORMATION?**

If you have any more questions or concerns, please contact your community or state health or



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environmental quality department, or contact ATSDR at the address and phone number below.

ATSDR can also tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

Toxicological profiles are also available on-line at www.atsdr.cdc.gov and on CD-ROM. You may request a copy of the ATSDR ToxProfilesTM CD-ROM by calling the toll-free information and technical assistance number at 1-800-CDCINFO (1-800-232-4636), by e-mail at cdcinfo@cdc.gov, or by writing to:

Agency for Toxic Substances and Disease Registry Division of Toxicology and Environmental Medicine 1600 Clifton Road NE Mailstop F-32 Atlanta, GA 30333 Fax: 1-770-488-4178

Organizations for-profit may request copies of final Toxicological Profiles from the following:

National Technical Information Service (NTIS) 5285 Port Royal Road Springfield, VA 22161 Phone: 1-800-553-6847 or 1-703-605-6000 Web site: http://www.ntis.gov/

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