Parathion, which usually refers to ethyl parathion rather than the closely related chemical methyl parathion, is one of a class of pesticides known as organophosphates. Among the most extremely acutely toxic pesticides, parathion is notorious for the number and severity of human poisonings it causes each year. In addition to its acute toxicity, there is evidence that parathion is a chronic neurotoxin, carcinogen, mutagen, reproductive toxin, immunotoxin, and can cause birth defects.

First introduced by Bayer AG of Germany in 1947, with a U.S. registration in 1948, parathion has a long history of human poisoning throughout the world. In the 1970’s approximately half the cases of world-wide pesticide poisonings were caused by parathion. EPA’s Pesticide Incident Monitoring System (PIMS), reported 1,283 human parathion poisonings between 1966 and 1980. Of these, 47 people died, 478 were hospitalized, and 743 received medical attention. In California, the only state which has consistently kept poisoning records, parathion ranks third in terms of frequency of poisonings and number of hospitalizations, and first for the number of days of victim hospitalization. Parathion has been banned in several countries, including Sweden and the United Kingdom.

In 1986, the agency sent registrants a preliminary notice of consideration for special review, indicating that the agency planned to put parathion into the Special Review process. By 1988, a workgroup within EPA had completed a document titled “Parathion Support Document”, which stated that “EPA has concluded that most uses of parathion must be cancelled because feasible measures to reduce acute exposure levels for both humans and birds are not available.” However, this document was never issued, and the working group within EPA had proposed that parathion be cancelled. The Assistant Administrator for the Office of Pesticides and Toxic Substances, Linda Fisher, said that she was considering the recommendation, but declined to state when she would make her decision regarding the future of parathion.

Parathion is a broad-spectrum insecticide used to control a wide variety of insects and mites on more than 80 crops. In addition, it is used in forestry, aquaculture, mosquito control and other non-crop uses. Application methods include aerial and ground spraying. It is classed as a Restricted Use Pesticide, for use only by certified applicators, because of its high toxicity and has no home or livestock uses.

The toxicity of parathion is caused by its metabolite, paraoxon, which is 50 times as toxic as the parent compound. Parathion, along with other organophosphates, binds irreversibly to the essential nervous system enzyme acetylcholine esterase (AchE), interrupting normal nerve impulse transmission. Acute oral
lethal doses (LD50) vary from 2 mg/kg in humans, to 3 mg/kg in dogs, to 5-30 mg/kg in rats. The probable oral lethal dose is between 7 drops and 1 teaspoon for a 150 lb. person. As little as one drop can endanger life if splashed in the eye. Young animals are more susceptible than adults of the same species. Female rats are more sensitive than male rats. Sensitivity is also increased by pregnancy.

The chemical is readily metabolized; after administration of parathion to rabbits, the chemical is rapidly excreted (85% at 6 hours) as p-nitrophenol in the urine. In humans, parathion is converted to paraaxon by the P450 enzyme system, and is then inactivated by the Circulating plasma enzyme paraoxonase. However, one study noted that half the Caucasian population has very low levels of this enzyme and is therefore highly susceptible to poisoning. In mice, pregnancy significantly lowers serum paraoxonase levels, heightening sensitivity to parathion.

The World Health Organization (WHO) has determined a human acceptable daily intake (ADD of 0.005 mg/kg based on rat AchE inhibition; however, EPA considers that this level may be too high, but has insufficient data on which to establish a no-effect level.

Parathion is also rapidly absorbed through the skin causing sweating and twitching within 15 minutes. Absorption is often increased by the presence of solvents in formulations. In addition, parathion toxicity may be increased by synergism with other pesticides such as atrazine, malathion, and bromophos.

Symptoms of exposure include slurred speech, loss of reflexes, and if exposure is high enough, convulsions and coma. Acute oral poisoning is often accompanied by nausea, cramps, vomiting, diarrhea, and loss of appetite, usually within two hours; inhalation may cause wheezing, chest tightness, bluish skin, small pupils and blurred vision. Long-term effects may bneuropsychiatric disorders, peripheral neuropathies (nerve cell degeneration) or myopathies (muscular degeneration). Disorientation, depersonalization, hallucinations, anxiety and abnormal brain (EEG) patterns may persist for weeks. Fatalities are usually caused by respiratory failure on the basis of central nervous paralysis.

Life-long studies in rats have shown serious eye damage (retinal atrophy) resulting from parathion ingestion. Similarly, Japanese field workers exposed to a range of organophosphates developed eye effects including myopia and degeneration of the optic nerve. The test rats also had an abnormal gait in the hind limbs resulting from sciatic nerve degeneration.

Poisoning in humans is diagnosed by pin point pupils, depressed plasma cholinesterase (AchE), parathion or paraaxon in blood or the metabolite para-nitrophenol in the urine. Patients treated within a few hours of exposure with the antidotes atropine and pralidoximine (2-PAM), generally together, may survive the effects of AchE depression. The diagnosis may be initially missed in parathion poisoned patients with pulmonary edema when no exposure history is available.

The chemical is teratogenic in frogs causing abnormal pigmentation, gastrointestinal development and notochordal (embryonic spinal chord) defects. Tests on guinea pigs exposed to parathion showed chromosomal breakage in germ cells, which could be an indication of its potential to cause birth defects. The frequency of chromosomal aberrations and sister chromatid exchanges (SCE) in lymphocytes were increased significantly in workers exposed occupationally to parathion, as well as other pesticides. Reported reproductive effects include resorption and low fetal weight in mice, increased mortality and decreased litter size in rats, and reduced sperm motility in pigs.

According to EPA, most mutagenicity tests were flawed, but a positive test for induction of DNA repair in human cells makes parathion a potential mutagen. Tests for point mutations, numerical and structural chromosome aberrations, DNA damage/repair, and in vitro transformation provide supportive evidence of carcinogenicity.

Parathion is carcinogenic in rats. Both male and female rats ingesting parathion had significantly elevated adrenal cortical adenomas and carcinomas. There were also significant trends for thyroid follicular cell adenomas and pancreatic cell carcinomas in treated rats. Initial review of another rat oncogenicity study reported an increased incidence of follicular cell adenomas of the thyroid gland in males. Upon re-analysis of the data the Agency decided that the rat study was negative. They also found the mouse oncogenicity study flawed. EPA classifies parathion as a class C, possible human carcinogen. In 1983, the International Agency for Research on Cancer found insufficient evidence to be able to classify parathion as to its carci-
nogenic potential.\textsuperscript{17}

Only one study examined the effects of parathion on the immune system. One-tenth of the oral LD50 resulted in suppression of the immune response in mice.\textsuperscript{1}

As with most AchE inhibitors, birds are more acutely sensitive than mammals to parathion.\textsuperscript{18} EPA noted 26 bird kill incidents which occurred throughout the year in the following states: CA, OK, TX, NC, GA, and NY.\textsuperscript{19} Numbers of reported dead birds ranged from 3 to 1,600, and involve many species including songbirds, waterfowl and raptors. However, few wildlife-monitoring studies have been performed.\textsuperscript{20} In addition, there is some indication of adverse effects on avian reproduction. While there is limited data on aquatic species, the chemical is extremely toxic to fish and aquatic invertebrates with median lethal concentrations (LC50) as low as 0.036 mg/l for some aquatic invertebrates.\textsuperscript{1}

Fresh water half-lives range from 43 to 170 days depending on the temperature and pH. Parathion has been found in the groundwater of three states, CA,\textsuperscript{21} MO,\textsuperscript{22} and ND.\textsuperscript{23}

Residues of parathion may persist in soil for many years.\textsuperscript{24} Studies have reported parathion residues in soil 16 years after the last application.\textsuperscript{25, 26} In addition, high levels of parathion, 15,370 ppm, have been known to persist for at least 6 years (the duration of the study) following a spill of parathion.\textsuperscript{27} EPA notes that, “In the field, parathion is normally permanently deactivated by chemical conversion to diethyl phosphoric add. However, under arid conditions, up to 30% of the parathion is converted to paraoxon.”\textsuperscript{19} In general, paraoxon is a photo degradation (breakdown via exposure to sunlight) product.

Applicator protection measures were first introduced in 1970 [EPA parathion support document], and in 1978 the agency restricted parathion use to trained, certified personnel and required full protective clothing including impermeable boots, clothing and gloves, and a respirator.\textsuperscript{28} EPA suggested that periodic blood or urine tests be done to assure that workers are not overexposed.\textsuperscript{11} Poisoning incidents indicate that acute systemic toxicity continues to be a serious problem for mixer/loaders, applicators and field workers in spite of extensive protective measures and increased Federal restrictions on its use. WHO recommends that unprotected persons be kept out of treated areas for 14 to 21 days after application.\textsuperscript{29} EPA's reentry intervals vary from 3 to 45 days depending on crop, application rate, and state.\textsuperscript{30} The chemical is retained on the surface of plants and fruit, clothing and mechanical equipment, all of which may remain toxic for days. Decontamination is difficult; articles known to have been in contact with parathion are best destroyed.\textsuperscript{1}

EPA's 1986 Registration Standard requires: 1) animal studies based on neural and retinal effects seen in earlier studies; 2) an oncogenicity study in mice; and, 3) a review of the follicular adenomas of the thyroid gland. The mouse oncogenicity study was received in 1991, and is under review.\textsuperscript{31} The neural and retinal effects study is due in April, 1991. The Agency is also requiring bird monitoring, residue data on the full range of crops for which tolerances have been established, and human exposure data measuring worker exposure levels by patch test and urinary metabolite analysis. There may be a risk from dietary exposure to parathion. Additional residue and toxicology data are needed to ascertain the extent of the risk from dietary exposure and to conduct a tolerance reassessment.

The sole U.S. manufacturer, Monsanto Chemical Co., discontinued production in 1987. Chemi nova Agro A/S of Denmark is the major basic producer.

\textbf{UPDATE: October 2007 Voluntary Cancellation}

Effective December 31, 2002 all parathion end use products were voluntarily cancelled, with last legal use on October 31, 2003. This was as a result of the high estimated risks based on the best information available to the EPA, and the registrants' decision not to support the data requirements for reregistration.

\begin{center}
\textbf{UPDATE: October 2007 Voluntary Cancellation}
\end{center}

Effective December 31, 2002 all parathion end use products were voluntarily cancelled, with last legal use on October 31, 2003. This was as a result of the high estimated risks based on the best information available to the EPA, and the registrants' decision not to support the data requirements for reregistration.
Parathion chemicalWATCH Factsheet Bibliography

15. International Register for Potentially Toxic Chemicals. 1989. Consolidated list of products whose consumption and/or sale have been banned, withdrawn, severely restricted, or not approved by governments, 3rd edition. UNEP / IRPTC, Geneva.

30 U.S. EPA. Personal communication with Dennis Edwards, Product Manager for parathion, quoting the Parathion label. Note that for cotton and most crops, including vegetables, reentry time is only 3 days. For apples, peaches, corn, olives, tree fruits, and nuts, reentry time is 6 days. For citrus and grapes, in CA, AZ, NV, NM, OK, TX, and UT, reentry times are 21 days for less than 4 lbs/acre, 35 days for 4-8lbs/acre, 45 days for >8lbs/acre, but only 5 days in any other state.