

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

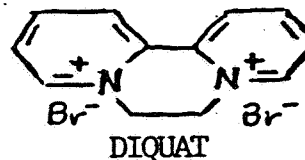
Region III - 6th & Walnut Sts.  
Philadelphia, Pa. 19106

SUBJECT: MUTAGENICITY OF DIQUAT

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FROM: BRUCE MOLHOLT, PH.D. (3HW12)  
Toxicologist, CERCLA Enforcement

TO: LARRY MILLER (3HW13)  
Acting Chief, TSCA/FIFRA Enforcement



On 14 June 1983 EPA approved Chevron's removal of a warning advising against swimming for 14 days in water sprayed with the herbicide diquat. This action has caused some consternation during the summer of 1984 in that citizens found themselves unwarned about diquat spraying as they had been in previous years. In several instances persons were using surface waters recreationally during diquat spraying.

In light of diquat's structural relationship to highly toxic paraquat and to genotoxic biphenyls, I decided to search the contemporary literature for research concerning the mutagenicity of diquat. Considering the results of several studies in which diquat is more toxic and genotoxic than paraquat, I suggest that EPA reconsider its lifting of the 14 day ban on swimming after spraying with all herbicides containing diquat.

Experimental data

Benigni and his co-workers in Rome tested the mutagenicity of diquat in six short-term test systems. Diquat was mutagenic in five of these systems, including bacteria, fungi and human cells as test organisms. The tests of unscheduled DNA synthesis in human epithelial cells is an indication of DNA damage and potential mutagenesis by various substances. The following results were obtained by Benigni et al. using grains of <sup>3</sup>H-thymidine incorporated per nucleus as an indication of unscheduled DNA synthesis:

UNSCHEDULED DNA SYNTHESIS IN HUMAN CELLS TREATED WITH DIQUAT

| <u>Treatment</u>            | <u>Grains/nucleus</u> |
|-----------------------------|-----------------------|
| None (control)              | 3.6                   |
| Diquat (20 µg/ml)           | 14.5                  |
| Diquat (100 µg/ml)          | 13.4                  |
| Diquat (1000 µg/ml)         | 16.6                  |
| Diquat (2000 µg/ml)         | 24.3                  |
| Nitrosoguanidine (15 µg/ml) | 54.4                  |

This experiment shows that diquat stimulates unscheduled DNA synthesis significantly above background levels and proportional to dose. It also shows that on a weight-per-weight basis diquat is about 5 percent as potent in induction of unscheduled DNA synthesis as the potent mutagen nitrosoguanidine.

Benigni and his co-workers' data are confirmed by independent experiments by Anderson et al. They used human cells transformed by SV40 virus and found that these were stimulated for unscheduled DNA synthesis by diquat.

Similarly Selyes et al examined teratogenicity and clastogenicity of Reglone, a herbicide which is 20 percent diquat. In control mice only one untreated female per 50 examined delivered malformed offspring. One intraperitoneal injection with 11 mg/kg Reglone (2.2 mg/kg diquat), however, induced 6 malformations per 50 deliveries, and, with 4 injections of 2.7 mg/kg Reglone (0.54 mg/kg diquat) 13/50 deliveries were malformed. Selyes et al removed cells for cytogenetic analysis from 10 embryos from each test group and found 9 percent chromosomal abnormalities in singly injected mice, 10 percent in multiply injected and 2 percent in controls. These experiments show that diquat is both a teratogen and clastogen in mice.

#### Diquat as compared to paraquat

Several experiments suggest that in all but lung toxicity, diquat is twice as toxic as paraquat. Whereas it takes 10 mg diquat to irritate a rabbit cornea (Brit. J. Indust. Med. 27, 51 '70) it takes 25 mg of paraquat to elicit the same reaction (Brit. J. Indust. Med. 23, 126 '66).

In the induction of 8-azaguanine resistance in bacteria, 0.1 µg of diquat is as effective as 0.25 µg of paraquat (Benigni et al).

And finally, using a very sensitive plant assay for diquat and paraquat, the chlorosis (chloroplast leaching) of duckweed, Funderburk and Lawrence found that 10 ppb of diquat caused 70 percent chlorosis in 11 days. whereas the same concentration of paraquat induced only 35 percent chlorosis.

These experiments measure eye irritation, mutagenic potential and chlorosis - three very different measurements of biologic effectiveness - and yet diquat is twice as potent as paraquat in all three.

#### Discussion and conclusion

The above discussion deals only with low doses of diquat or dilute solutions. There are many other papers which describe diquat's acute (lethal) toxicity at high concentrations (the LD50 in mice is 22 mg/kg), but these do not simulate the aquatic environment in which diquat is most likely to be encountered by humans. Diquat is generally applied to lakes at 0.1-1.5 ppm. Despite statements to the contrary, some experiments show as much as 10 percent activity remaining 14 days after application. Aquatic use of diquat is much different than land use where diquat is quickly and irreversibly adsorbed to soil.

In that several different experiments, including use of human cells, clearly indicate diquat's mutagenicity, it may be prudent for EPA to

reconsider rescission of the 14 day ban between spraying and swimming until this pesticide can be thoroughly tested for human genotoxicity.

References

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*Product*

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Meadville Tribune  
MEADVILLE, PA.  
AM-16,223

LETTER:

## Diquat Fears Raised

Editor of the Tribune,

On June 19 and 20, the Bureau of State Park and Department of Environmental Resources (DER) treated Conneaut Lake with 125 gallons of Diquat herbicide h-a, a desiccant defoliant for aquatic plants.

The Environmental Protection Agency (EPA) claims it is safe to swim in treated water, having approved the deletion of the swimming restriction on the weed killer label in June 1983 and allowing swimming following application without a 14-day waiting period. Keep in mind that there is no change in the chemical makeup of the herbicide; just compare the old label with the new one and read the precautionary statements, the hazards to humans and domestic animals warnings. It says, "Do not use the treated water for...domestic purposes for 14 days after treatment." Safe?

The National Clearinghouse for Poison Control Centers says of Diquat:

"Toxicity: the concentrate is corrosive and a primary skin irritant. The amount of Diquat which would cause death in man following a single oral dose has been estimated at six to 12 grams.

"Symptoms and Findings: ingestion, concentrated solutions of Diquat cause severe irritation to the mucous membranes of the mouth, pharynx, esophagus and stomach. This may be followed by ulceration and perforation. There is usually recurring vomiting and, after large doses, restlessness and hyperexcitability. Death from Diquat poisoning is accompanied by thickening of the alveolar lining of the lungs and by gross abdominal distention due to retention of gas and fluid.

"Inhalation: exposure to spray mists may cause skin irritation, nasal bleeding, irritation and inflammation of the mouth and upper respiratory tract, cough and chest pain. Skin: contact may cause severe skin irritation and burning; symptoms similar to those following ingestion may occur from skin absorption especially with repeated contact

Eyes: contact with dilute liquid may cause reversible eye irritation."

These are only a few of the short-term effects.

Consider these additional facts: recent studies have been published which have indicated that Diquat is a mutagen; the chemical herbicide caused mutation in concentrations well below the level of concentration used in Conneaut lake. Studies have also found that liver damage from exposure to Diquat can result, and that no level of concentration is known to be positively safe in this regard. Still safe?

If you were swimming or water skiing in the lake on June 19 and 20, you were probably exposed to this herbicide. My family, four invited neighbors, and myself were using the lake on the 19th. None of us was aware of the chemical treatment until it was too late. Both of my daughters had medical problems, one with a bad eye infection, the other with an ear infection and slight rash. The younger neighbor boy had a severe rash that required a doctor's attention. I know of several others who had or still have medical problems that were using the lake these two days. I can assure you we would not have chosen to be there if we had known about the chemical treatment.

Who is responsible? DER, the bureau of state parks, our state lawmakers? I'm sure the people responsible were not in the lake those two days. The next time they decide to treat the water with Diquat, I'll personally extend my invitation to them to ski behind my boat. You'll not see my family in the water.

LARRY WALKER

699 Davenport St.  
Meadville, Pa.

