Monsanto

FROM (NAME & LOCATION): M. F. Baber - St. Louis

DATE: April 8, 1971

CC:

SUBJECT: Toxicity of Halogenated Polyphenyls

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df: Brom. Polyphenyls-Toxicity

SUMMARY:

This memorandum defines and discusses the recommended toxicity testing program for new brominated and chlorinated polyphenyls, and fibers and resins containing these compounds. The recommendations are based upon the results of a series of meetings between the Medical Department and representatives of Monsanto divisions involved.

Product and applications testing can proceed on terphenyl (and quaterphenyl) compounds. However, an initial test program to prove the environmental acceptability of compounds of commercial interest should be initiated as soon as possible. Such a test program would cost about $25,000 per compound, with an elapsed time of 6 - 9 months. The total toxicity testing program for any one new commercial compound would be $50,000 - 100,000.

Strong consideration should be given to discontinuing product and applications testing of halogenated biphenyl compounds until some other company, such as Dow, demonstrates environmental acceptability of these compounds.

The Organic Chemicals Division should be in a position by early June to state its interest in participating in a toxicity testing program on brominated polyphenyl compounds. A review with other divisions involved is tentatively planned at that time.

DETAILS ON COMPOUNDS

The H&P and Textiles Divisions are testing highly chlorinated terphenyls, highly brominated biphenyls, and highly brominated terphenyls for use as non-reactive additives for future commercial

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fire retarded molding resins and synthetic fibers. The Organic Chemicals Division produces chlorinated biphenyls and terphenyls, and is considering the production of brominated polyphenyls (biphenyls, terphenyls, etc.) for internal and external consumption. Recent problems with highly chlorinated biphenyls (PCB's) have made everyone wary; consequently, a series of meetings was held with the medical department to clarify the corporate attitude toward new halogenated polyphenyl compounds and their possible commercialization.

Highly chlorinated biphenyls (PCB's) concentrate in certain marine life and have a resulting detrimental effect on the reproduction capabilities of certain fish-eating birds. Consequently, highly chlorinated biphenyls should not be considered for any application in which they might enter the environment. In other words, they should not be evaluated for non-reactive resins and synthetic fibers applications either by Monsanto or by other companies.

Chlorinated terphenyls are still being tested for toxicity and environmental effects. However, to date, they have been found harmless and can be considered for commercialization both as chemicals and as additives for Monsanto resins and synthetic fibers.

Brominated biphenyls are too close in structure to the PCB's for corporate comfort. They may be found to be toxicologically and ecologically acceptable. However, it is recommended that no products containing brominated biphenyls be sampled outside of Monsanto until they at least pass an initial battery of tests. These would be equivalent to tests (1) - (7) in the attached test schedule. Dow Chemical and other potential suppliers should be requested to furnish such toxicological test data as soon as possible.

Brominated terphenyls are felt to have a better chance than the biphenyls of passing necessary toxicity tests. Consequently, these compounds and products containing them can be sampled outside the company. However, as soon as possible, tests (1) - (7) in the attached test schedule should be performed on compounds of commercial interest.

Brominated quaterphenyls were discussed only briefly, as it is not known whether they can be produced with acceptable properties. If so, they would stand a better chance than the biphenyls or terphenyls of being toxicologically acceptable, since they should be considerably more inert. They would have to pass some toxicity test program, but probably not as extensive as that in the attached table.

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TOXICITY TESTING PROGRAM

The table on the next page outlines the recommended toxicity testing program for brominated biphenyls or terphenyls.

Test 1., activated sludge, is in progress for a 65% brominated terphenyl and a 76% brominated biphenyl (hexabromobiphenyl). If neither are extremely biodegradable, as is expected, then tests 1. - 7. will be required on any product of commercial interest. If either proves to be extremely biodegradable we will be encouraged. However, then activated sludge studies will be required on 76 - 81% brominated terphenyl and/or 81% brominated biphenyl (octabromobiphenyl) as these are the products of high commercial significance. Also, based on chlorinated biphenyl results, it is strongly speculated that the more highly brominated polyphenyls will be less biodegradable. In converse, fortunately, they also appear less toxic as they are less soluble in solvents and in body tissue.

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TOXICITY TESTING PROGRAM FOR BROMINATED POLYPHENYLS
(In rough order of Testing)

	Estimated Cost, $	Lapsed Time Weeks
BIODEGRATATION		
1. Activated sludge (1)	$ 3,000	9
ACUTE TOXICITY		
2. Acute mammalian toxicity	500	5
3. Acute fish toxicity	600	4
ANALYTICAL		
4. Analytical methodology (1)	7,500	6
5. Water solubility (1)	400	1
BIOLOGICAL/ENVIRONMELTAL EFFECTS (4)		
6. Subacute fish toxicity and biological magnification (1)	3,000	18
7. Chicken reproduction (1)(2)	8,000	26
GASEOUS PRODUCTS AND SMOKE		
8. Toxicity of degradation products	2,500	4
9. Smoke generation (3)	--	--
ANIMAL EFFECTS - REQUIRED (4)		
10. Subacute 90-day rats and dogs	16,000	26
11. Human patch (assume 2 fabrics)	5,200	9
12. Teratology, rats	1,800	13
ANIMAL EFFECTS - QUESTIONABLE		
13. Rat reproduction	17,000	78
14. Mutagenicity - rats	3,500	13
15. Chronic inhalation studies	15,000	--

NOTES:

(1) Can skip most of tests 4. - 7. if compound proves very biodegradable.

(2) Can skip test 7. is there is no significant biological magnification in test 6.

(3) Test parameters not yet defined by the industry.

(4) Tests 6., 7., 10. and 12. do not include costs of sample analysis which could be $5000 - 10,000.

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Test 2. (acute toxicity) and 3. (acute fish toxicity) must be run on all compounds. 76% bromoterphenyl was ruled non-toxic by test 2. 65% bromoterphenyl was also relatively non-toxic, but showed a higher skin absorption toxicity than desirable. Insufficient data exists on the bromobiphenyls. The only known acute fish toxicity test was run by Dow on octabromobiphenyl (OBB); it was inconclusive because of the low solubility of OBB in water.

Test 4. concerns developing an analytical method for measuring brominated biphenyls and terphenyls in small quantities - down to parts per billion. This is required for analyzing the results from test 6. and some later tests. This may be a significant stumbling block to the program. Dr. Bob Keller estimates a 50% chance of success of developing an analytical technique for brominated terphenyls; this effort would require three man months and would cost $5,000 - $7,500. An analytical technique for bromo quaterphenyls, short of radioactive tagging which is costly indeed, would be even more difficult to develop.

Test 5. water solubility is needed as background information for any fish toxicity work.

Test 6. gives both a measure of residual fish toxicity, and more importantly, biological magnification in fish tissue. It is the presence of biological magnification which allows the PCB's to build to the level where they effect the enzymatic functions of certain water fowl. If significant biological magnification occurs with the brominated products, then test 7., chicken reproduction, must be run to determine if at high concentrations whether the compounds cause the egg shells to become thin. If the chicken egg shells become thin, the compound is unacceptable for use in fibers and molding resins. If not, we will be encouraged enough to proceed with applications testing, but will be concerned lest the later animal tests show toxic effects.

If on the other hand the product shows no biological magnification, then test 7., chicken reproduction, can be omitted entirely.

Once tests 1. - 7. are completed without the compound being disqualified, then applications testing can begin in earnest.

On any fiber or polymer which is being seriously considered for commercialization tests should be performed on the toxicity of degradation products and on smoke generation. MRC has designed a test to measure the composition of degradation products and the relative smoke generation upon burning. The cost would be about $2,500 if four fabrics and/or polymer compositions were tested.

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Once commercialization was close at hand tests 10. and 11., animal subacute toxicity and human patch, should be run. The final tests may or may not be required depending upon the area of application, new laws passed, and the results of prior tests.

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