CONFIDENTIAL

TO: DR. J.W. BARRETT.

19th August 1955.

DVNH/MEB

AROCLORS -
TOXICOLOGICAL EXAMINATION

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Further to my memo of 9th August, I propose to summarise the present position on Aroclor vapour toxicity as an essential background to our policy and to our consideration of the Battelle proposal for a programme of toxicological work.

I have indicated in my summary of the two reports by The Kettering Laboratory that prolonged exposure (7 hours a day for 150 days) to Aroclor 1254 vapour at 1.5 mgrm./m^3 caused slight but positive signs of injury in test animals and that similar experiments with Aroclor 1242 gave negative results at 1.9 mgrm./m^3. As I see it this positive result with 1254 would be construed by Public Health Authorities as an indictment of Aroclors as a class, and the negative result with 1242 would not rank as a clearance for that particular chlorinated diphenyl. To upset the one positive result with 1254 would require much more than a simple re-investigation, since it would be necessary to demonstrate by an even more exhaustive and searching investigation that the Kettering observations were mistaken. Even then, the work would probably not be decisive until confirmed by an independent authority.

During the near future, at any rate, our consideration of the suitability of Aroclors for specific applications must be governed by this finding that prolonged exposure to Aroclor vapour at 1.5 mgrm./m^3 can produce damage to the liver and kidneys of test animals. In translating this finding to the human being it is the recognised practice to employ a safety factor of 10; in other words when the maximum, safe concentrations for test animals has been located, the corresponding value for the human being is taken as one tenth of it. With 1254 we now know that 1.5 mgrm./m^3 is <u>above</u> the maximum permissible concentration for

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test animals so that the maximum for human beings must be placed below 0.15 mgrm./m^3, and must be regarded as applying to all Aroclors, on account of their similar chemical constitution.

Our own analytical work with a room painted with Aroclor 1248 plasticised Lustrex Latex paint affords evidence that Aroclor concentrations of the order of 0.5 mgrm./m^3 can prevail for a month; we have not so far attempted to develop the more refined analytical technique necessary to determine with reasonable precision concentrations in the range of 0.1-0.5 mgrm./m^3. This development would be a difficult assignment and when available it would only permit us to determine the time to reach 0.15 mgrm./m^3 and hence the time during which a person could be exposed to concentrations greater than what must now be regarded as the maximum permissible.

Previously on the basis of published work the value has been taken variously at 0.5 or 1 mgrm./m^3 and Monsanto has normally used the higher figure. On that basis it could be argued that exposure to a concentration at or above the maximum permissible would be of short duration and that any hazard was of marginal significance.

However, we now have to reckon with a fairly long exposure to concentrations above the new maximum, and hence the hazard must be rated much greater. There is yet a further consideration that is always taken into account by Health Authorities, and this relates to the idiosyncrasy factor. So far we have considered the <u>average</u> human being, but there will always be a minor proportion more susceptible than the rest. This may be due to the natural variability of resistance or predisposition existing among healthy individuals, or to functional disability, and in assessing a human hazard consideration is always given to those individuals who are more likely to suffer injury; in this case presumably those possessing impaired livers and kidneys would be most likely to suffer first.

If the argument I have presented above is accepted then we must now line up with M.C.C. in withdrawing our recommendation that Aroclors be used as plasticisers in Lustrex Latex paints. As regards the use of Aroclors in P.V.A. paints, we have so far made no measurements of Aroclor concentrations in painted rooms, but I see no reason for believing that materially reduced concentrations would be found.

We have still to examine the position of Aroclors in ordinary paints. Here I have argued that the rate of volatilisation will be greatly reduced and probably governed by the rate of migration within the dry paint. It now seems possible that a hazardous concentration could

be attained in a room in which a large area is painted with Arcolor-containing paint. Certainly we must say that these paints must not be used on hot surfaces such as radiators and hot-water pipes.

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1. TOXICITY COSTS

Dr. Kelly first outlined the various schemes of toxicity tests that M.C.C. arrange to have conducted on their products.

Minimum LD_{50} tests cost $50-75.
If the product is liquid, dermal tests and ocular damage tests are also carried out bringing the total cost to about $200. Inhalation, saturated air at room temperature or volatalisation from a heated plate cost a further $75. Sub acute toxicity, one-tenth LD_{50} test for 10 days would bring the whole total to $400.

The 90 day test, orally to two species of rats and one of rabbits, together with 20-30 day inhalation tests cost $2,000. If the products are to be used as food wraps for meat, etc., then extraction studies with lard and water with 2 years feeding to rats and 1 year to dogs cost a further $30,000. For foods such as bread, etc., this full test is not required although it can be called for by the appropriate State or Federal Department.

The Medical Department of M.C.C. is allocated $20,000 for arranging the $400 tests, $10,000 for further tests if required and $5000 for any odd work. If the tests cost more than $400 it is billed back to the appropriate Division.

It was estimated that it would cost M.C.C. some $200,000 a year to carry out their own toxicity investigations and consequently the work is farmed out to consulting firms and costs up to $40,000. In the light of these figures there is no justification for setting up toxicity facilities by M.C.C.

Patch tests are not of very great value.

2. AROCLORS ELECTRICAL

The indications are that there are no serious toxic hazards in this application. The electrical industry has never requested or permitted Aroclor vapour levels to be determined in their plants. Capacitor impregnation is always carried out in fan exhausted closed ovens.

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3. AROCLORS - HEAT EXCHANGE

There has been some trouble in the use of Aroclors as heat exchange fluids but this is always associated with poorly designed and leaking equipment. In one case three people suffered liver damage in about a week's exposure, but the vapour concentration must have been excessively high as the equipment was full of leaks and was in a badly ventilated shed. Dr. Benignus keeps a careful check on sales of Aroclor and if the replacement rate is high he has the situation investigated.

4. AROCLORS AND PHOSPHATES - HYDRAULIC

M.C.C. had little to add to present published knowledge. They produce low ortho T.T.P. from cresol containing 4% ortho cresol, for plasticisers and hydraulic applications, and high ortho content from 20% ortho containing cresol for use in petrol. Toxicity does not appear to be important, they have had no trouble in the plant even with the high ortho material. Leaks in equipment should be prevented and exhaust fans fitted if the equipment demands them. They have had no complaints regarding Pydraul F.9. Aroclor 1242 is slightly more volatile than Aroclor 1248 and consequently precautions will have to be somewhat tighter.

5. AROCLORS - LATEX PAINTS

M.C.C. had first considered that styrene based paints could not compete on price or performance with the styrene - butadiene paints. Also, having found that the vapour concentrations in a painted room were higher than the permitted level, they barred the use of Aroclors 1242 and 1248 in Lustrex latex paints. The use of higher Aroclors with other plasticisers had not been considered. On the basis of the M.C.L. results no danger should exist in rooms painted with Aroclor 1248 plasticised latex paints but no case could be presented in court for such paints, should it happen that someone using the painted rooms contracted liver damage from some other cause or injury, connected it with Aroclor and brought action against the Company. It is therefore a question of company policy whether to recommend Aroclor as Lustrex latex plasticiser in view of the risk of the above taking place, although this risk may be negligible.

M.C.C. are running inhalation tests at 3 mgs. per cubic metre per 8 hour day on animals. At 7 mgs. per cubic metre

concentration, animals had suffered liver damage. A limit of 1 mg. per cubic metre is quite safe for plants working on 8 hour shifts.

The wire covering industry has now changed completely from chlorinated naphthalenes to Aroclors on account of reduced toxicity.

6. SKYDROLS 7000 and 500

M.C.C. had been somewhat over optimistic about Skydrol 7000 in stating in the Bulletin that it is non-toxic as its level is of the order of Skydrol 500. However, they had not received any complaints regarding skin troubles etc. in the case of either fluid. The inhalation of the vapour or spray in a plane should cause no trouble even if extended to the time required to bring the plane to its landing point. In the case of prolonged inhalation it is no worse than mineral oil. There should be no necessity for safety precautions in handling the fluids if ordinary personal hygiene measures are adopted, gloves and barrier creams are of doubtful value.

7. SANTICISER 141 AND B.16

Santicizer 141 is safe as a food wrapper plasticiser based on the two year test. It is not absorbed nor metabolised, but it is more extractable than B.16. It would be toxic if administered intravenously. The latter is a safer material to use in food and meat wrappers, it has been fed to rats for 2 years at 20,000 p.p.m. of diet without ill effect. Dr. Kelly is however rather critical of this 2 year test. Santicizer E.15 is in the same category as B.16. D.O.P. has not been approved as it is more easily extracted than 141.

8. PHENYL PHENOLS

The only data available is that published by Dow.

9. DIPHENYL

Diphenyl is not permitted in the States by the Food and Drug Committee but nevertheless it is still sold there for citrus fruit preservation and no complaint has yet been lodged. A

comprehensive toxicity evaluation costing $40,000 was initiated by the Ford Reneer Craft Board Institute but the standards were set too high and diphenyl failed the tests. A further $36,000 will be spent on another evaluation in which the metabolism of the chemical in dogs will be studied. M.C.C. are subscribing $5,000.

10. METHYL SALICYLATE

The material is not a highly toxic substance and no difficulties have arisen from its use as a food flavouring agent. However products containing over 5% should be labelled "Use other than as directed may be dangerous and the product should be kept out of reach of children to prevent accidental poisoning".

11. SACCHARIN

An extensive investigation was carried out by the Food & Drugs Committee some two years ago on a number of sweetening agents, Saccharin and Sucaryl were cleared without reservation.

12. ASPIRIN

Aspirin can cause poisoning in children under three years of age due to their inability to metabolise the compound. Under certain conditions they can accumulate the aspirin in the system and elevation of temperature, instead of lowering, occurs, often with unfortunate results. Labels should be marked "Not for children under 3 years of age".

14. SODIUM BENZOATE AND BENZOIC ACID

Dr. Kelly knew of no information on the toxicity of these materials other than the mammoth work put out by the U.S. Department of Agriculture in 1909 which gave the comprehensive results of three independent investigations on the benzoates and which gave a complete clearance to these substances. He suggested that adverse comments suggesting that the benzoates were not as harmless as first thought had been spread around by competitors with potential new food preservatives.

With regard to the forthcoming enquiry by our own Ministry on food preservatives in which the benzoates will be reviewed, he suggested that we write to the M.C.C. legal advisor, Mr. Charles Caspari, Jnr.

15. HYDROXY BENZOIC ACIDS

Dr. Kelly has no information.

16. SALICYLAMIDE

The severe reaction reported by Malmö General Hospital is quite consistent with specific drug allergy. There is no evidence to doubt the low toxicity figures quoted for the material but the "under 3 rule for children" should also be applied.

17. PENTACHLORPHENOL FORMULATIONS AND SANTOBRITE

Weed-killing formulations containing penta have caused the death of three Porto Ricans, one Hawaiian and one Australian. In all cases the men were inadequately clothed, their legs became heavily coated with the spray and excessive skin absorption must have resulted. The symptoms were severe liver damage. St. Louis would be prepared to carry out tests on our 15% emulsion concentrate and Development will forward a sample to Dr. Kelly. Our literature should detail the necessary precautions. St. Louis are writing a new bulletin on toxicity of penta products.

18. SOPANOX AND THIURAD

Thiurad is a skin irritant and sensitiser, its oral toxicity is higher than Actamer and is not suitable for use in soap. Also its incorporation into self-sterilising PVC sheet has shown it to have skin irritant properties. M.C.C. have a better material than Actamer on the stocks.

Little information is available on Sopanox, it has been used in one hand lotion, but is not recommended for use in dentifrice as its long term action on enamel is unknown.

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19. ISOCYANATES

Dr. Kelly will be visiting Bayer and will pass on any information he acquires. According to I.C.I., 1.5 naphthylene diisocyanate is a strong asthma producer.

20. SANTOCEL AND SYTON

Early toxicity evaluations of Santocels with rats had given misleading results. It is now reasonably certain that Santocel does not cause silicosis in animals although it does cause some degree of fibrosis and irritation in the lungs. Du Pont now label their product "Caution - harmful dust" and M.C.C. use a similar phrase to the effect that the material should be handled with care and users should not expose themselves unnecessarily to the dust.

Although Syton does not produce silicosis, it has been shown that it tends to aggrevate tuberculosis. Animals who have been given a sublethal dose of tuberculosis from which they would normally recover, die when subjected to doses of Syton spray.

Extensive sampling tests of the air of numerous U.S. factories using Syton, failed to detect the presence of Syton. In India the conditions in the factories are very favourable to the formation of Syton dust and the mills should be cautioned to take greater care in their processing and to supply their workers with masks.

21. AROCLORS 4465 AND 5460 IN AGRICULTURAL FORMULATIONS.

These Aroclors act as insecticide bonding agents on the leaf and increase the activity of the preparations. They are mostly chlorinated terphenyls and have greater toxicity than the lower members.

It is difficult to decide whether there is any hazard in using these compounds in greenhouse sprays as the conditions as to quantity sprayed and the size of the droplets is so indeterminate. Aerosol sprays giving fine droplets will have a long suspension time in the air.

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