

Monsanto

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November 29, 1976

Dr. Jerry M. Johnson
Acting Chief, Criteria Documentation, Section 1
NIOSH, DCDS, CDB, RM 142
4676 Columbia Parkway
Cincinnati, Ohio 45226

Dear Dr. Johnson:

Attached are answers to the questions on the draft criteria document concerning occupational exposure to polychlorinated biphenyls.

We hope our comments are helpful and appreciate the opportunity to participate in the preparation of a responsible criteria document.

Sincerely,



W. B. Papageorge
Mgr., Product Acceptability

WBP/ken

attachment

DSW 019375

POLYCHLORINATED BIPHENYL EXTERNAL REVIEW QUESTIONS

1. The document inadequately documents industrial exposure related effects of PCB. It also inadequately defines clinical tests which could be used to monitor for potential adverse effects of PCB exposure among the industrial population. The document dwells at great length upon the effects observed in a population of Japanese citizens who were accidentally exposed to an acute dose of PCB in a cooking oil. No relation is established between this accidental acute oral exposure to a relatively high concentration of PCB and industrial type exposures. No relationship is established defining relative body burdens resulting from acute oral exposure versus other routes of exposure, dermal absorption and respiratory, that are more likely to occur in an industrial environment. Another study given seemingly unwarranted consideration, involved an unpublished report of an epidemiological study conducted among a group of research workers with some unknown previous exposure to PCB. No sound basis has been established to support the contention that PCBs are human carcinogens. It is suggested that efforts be extended to accurately assess the clinical health of U.S. workers exposed to PCB.
2. In studies with rodents and subhuman primates the most sensitive target organ was usually found to be the liver. In these studies the dietary level which did not produce an effect on the liver was between 1 and 10 ppm. Based upon these studies the most probable toxic effect of excessive PCB exposure would be chronic hepatic injury.
3. From the manner in which the document is put together it is impossible to tell if the recommended standard is based upon a logical scientific extrapolation of the information cited. Specifically, no attempt is made to relate the body burdens which would result from an industrial inhalation or dermal exposure to those obtained from animal experimentation or the usual data following oral administration.

Chapter V consists of a series of data relating the toxic effects observed after many different types or routes of exposure. It then states that on the basis of all this data the environmental limit should be 0.05 mg/M³ of PCBs in air. There is no logical support for the stated limit as based on the industrial usage this document is intended to relate. There has been no evidence shown to indicate that, as inferred on lines 4071-4072, "teratogenicity, fetotoxicity and carcinogenicity has occurred to man and to laboratory animals when they have been subjected to air-borne PCB levels below the current standard of 1.0 mg/M³ (42% chlorine)."

- 4a. To be supportable a standard must be based on the application of a safety factor to experimental animal data and/or upon the utilization of previous work history exposure concentration and clinical worker monitoring data. Which of these was used in establishing this standard is not clear. Specifically, the limit of 0.05 mg/M³ has not been supported by any data relating industrial worker exposure to clinical effects. In fact, the arrival of 0.05 mg/M³ as a "safe" level has not been explained at all.
- b. The document on line 3929 states that the current PCB standard is based on an 8-hour dermal exposure. This is not entirely correct.

The current standard does include a "skin notation" which refers to the potential contribution to the overall exposure by cutaneous route or particularly by direct skin contact. An environmental limit for air-borne material cannot totally prevent direct skin contact with material and the resulting dermal exposure. This concern has been aptly addressed by the ACGIH TLV committee on line 3925 by their reference to the fact that the current standard may not guarantee protection against dermal effects. The recommended environmental limit cannot guarantee such also since workers can still put unprotected hands in the material if they wish.

- c. Inadequate information exists to properly evaluate the need for and type of protection for the pregnant worker.
 - d. Until better scientific evidence is brought forth supporting a necessary change in the current OSHA standard on PCBs, no justification exists for modifying the existing environment limit.
5. We recommend that the current users of PCBs, capacitor and transformer manufacturers, be consulted regarding feasibility of compliance.
 6. To exclude biological monitoring in a standard for a material known to accumulate in fatty tissues would not appear advisable.

Biologic testing is an acceptable monitoring device if it is shown that a reasonable correlation exists between body burden, detrimental health effects, and degree of worker exposure. Biological monitoring may well give an indication of dermal exposure and degree of skin absorption that might not be evident through the use of air monitoring.

7. We assume that if the composition of PCBs is unknown, the sample chromatogram does not match the chromatogram of any commercial PCB standard mixture. In this case, measurement by electron capture gas chromatography is inadequate for two reasons. First, interferences may be present which may account for the differences in the chromatograms. Secondly, as pointed out in Table I of the draft, electron capture detector response varies by orders of magnitude for different PCB isomers. Hence, the analyst would not know what response factor to apply, even using the weight factor technique of Webb & McCall (see attached comments for line 5354).

Therefore, when the PCB composition is unknown, a more specific and accurate technique must be used. We recommend using GC/MS in the selected ion monitoring mode as the detector device. The parent ion and a characteristic fragment ion are monitored for each PCB homolog. This technique is much less subject to interferences and is more accurate because MS response factors are nearly constant. GC/MS detection can be used with samples collected on Florisil if sensitivity is adequate. If sensitivity is inadequate, samples should be collected on a porous polymer sorbent such as Tenax GC. Collected components are then thermally desorbed directly into the GC/MS for analysis.

8. In those cases where the sample chromatogram matches a standard PCB chromatogram, the sampling procedure is adequate. However, as mentioned in 7., we recommend sampling with Tenax GC as a more general method. Collected components can be thermally or solvent desorbed from Tenax GC. For further details, see pp 147-160 of the transcript of the Second NIOSH Solid Sorbents Roundtable in December, 1973.

9. No, several deficiencies should be corrected. See attached comments relative to lines 5252, 5253, 5258, 5273, 5291, 5292, 5303, 5310, and 5320 of the draft.
- 10a. We recommend collection on Tenax GC adsorbent, thermal desorption and measurement by GC/MS. See 7., 8., and attached notes.
- b. See attached comments, especially the notes relevant to lines 5354, 5381, 5396, 5410, 5460, 5533, and 5590 of the draft.
- 11a. Annual comprehensive medical examinations are considered appropriate.
- b. The medical requirements listed in the document under Section 2 are patterned after the criteria document on Tetrachloroethylene. It would seem that the medical tests for PCB exposed workers could be more specific for that particular material. Pulmonary function tests should be included as a check on capability of wearing respiratory protective devices.

Contrary to lines 202-203, medical surveillance should be made available to all workers occupationally "exposed" to PCBs who contact the material and yet not be "exposed" on the basis of the NIOSH definition given on lines 176-177.

12. There is no persuasive evidence supporting the "cancer suspect agent" labelling all PCBs, therefore such labelling is inappropriate. Warning signs should be posted in those areas in which workers are exposed above some specified limit or where potential skin contact is possible. To be functional a warning sign must inform the reader of specific effects of a material. PCBs have relatively mild irritant properties and has not been associated with acutely toxic effects. However, tissue accumulation and target organ effects may occur following prolonged exposures above the established permissible limits. A meaningful sign would warn of potential tissue PCB accumulation and indicate avoidance of skin and eye contact.
13. Considering that the concentration limits as listed in Table I-1 represent the protection factors as shown below, the limits are considered to be appropriate and consistent with the respirator decision logic used in the Standards Completion Project.

Along with the protection factor limits are listed various additional respirator types which should provide adequate protection when used in areas of respective air contaminant concentrations.

Concentrations of
Polychlorinated Biphenyls
0.5 mg/M³ or Less (10x)

Respirator Type
(Modifications to Table)

3. Chemical cartridge respirator with replaceable cartridges approved for organic vapors and mists and half-mask facepiece.
4. Gas mask, chin-style or front or back mounted organic vapor and mist cannister.

DSW 019378

Concentrations of Poly-chlorinated Biphenyls cont'd.

2.5 mg/M³ or Less (50x)

5.0 mg/M³ or Less (100x)

Greater than 5.0 mg/M³ (100x)

Respirator Type (Modifications to Table) cont'd.

3. A gas mask with a full facepiece and front or back mounted vapor cannister with high efficiency filter.

(No modification)

(No modification)

14. Line 292: Detectable level is mentioned. Since the detectable limit of PCBs has not been addressed, this level is meaningless. It would make more sense to reduce air-borne concentrations of PCBs to below the (TWA) environmental limit or permissible exposure limit.

Lines 379 through 382 should be deleted since it seems unnecessary to have escape type devices available in all areas of "potential" exposure where the exposures might be brief at low or moderate levels. Escape type devices are generally made available in defined high risk areas containing potentially hazardous operations involving extremely toxic substances. The document does not provide data which supports PCBs as being considered extremely toxic.

Earlier comments addressed the modifications in Table I-1 on respirator types vs. concentration limits.

15. Line 405: Do hazards imply only health related hazards or environmental hazards also?

In general, Section 5 provides adequate avenues for communicating work hazards to workers.

16. The work practices and control procedures are considered adequate for the protection of workers.
17. The recommended record retention period appears to be appropriate.
18. Additional research is needed in the following areas:
- Comparative data on the PCB body burden resulting from oral, dermal and inhalation exposures.
 - Comparative metabolism studies of an homologous series in humans, non-human primates and rodents. These studies should include both a characterization of the metabolites formed and kinetic studies to determine the rates of mobilization and excretion.
 - Clinical evaluation including liver function tests on industrial populations with previously documented PCB exposure.
 - Epidemiological studies on major populations of PCB-exposed workers.
19. Attached is a report compiled by Monsanto and distributed in November, 1975 to representatives of concerned governmental agencies, (NIOSH, OSHA, EPA, FDA, NCI, NIH) relating to histopathological evaluation of livers from rats treated with PCBs.

COMMENTS ON SAMPLING AND ANALYTICAL METHODS

Minor comments are on the original NIOSH draft.

General comments: In using trade names, the document should be consistent. Any shorthand such as dropping registration notation should be documented at the earliest opportunity and then a standard format adopted thereafter e.g. Aroclor^R

Florisil^R

Environmental Sampling and Analytical Methods

3714evaluated under laboratory conditions using aerosol generation techniques. Field studies were also performed in a PCB environment containing aerosol and vapor components.

The statement as it stands leaves open the question of aerosol or vapor studies. The document should be completed by inclusion of this information in a manner similar to the above amended statement, and expressing the true nature of the exercise. Both aerosol and vapor concentrations must be included.

3724 Earlier in the text, 2 solvents are mentioned along with the use of
-3726 single and multiple impingers.

Which solvent was used should be clarified (toluene or ethylene glycol) and the number of impingers.

The conclusions reached imply a study using an aerosol of PCBs or an equilibrated vapor environment. Is this true?

3737 to use when personal sampling for PCBs.

This circumvents other techniques such as area monitoring for calculating effective exposures.

3738 NIOSH has not tested all available solid sorbents (e.g. porous polymers). Hence, this line should be reworded to reflect only those methods tested.

3752 Electron capture gas chromatography is the most widely used method, but not necessarily the "preferred" method. For example, the wide variance in response factors referred to in Table I is a distinct disadvantage.

3801 In this day, it is not possible to eliminate a method based on the lack
-3803 or expense of a computer. In many small companies, the OSHA requirements will rapidly force the purchase of such a unit for many applications.

3809 One might prefer NBS as a repository for "standard" samples.
-3810

3824 Perchlorination should definitely not be used to quantitate PCBs. We have confirmed that not only biphenyl, but also substituted biphenyls, cause large positive errors. At least one of the replacement fluids for PCBs in capacitors is a substituted biphenyl (Chemical and Engineering News, p. 25, Nov. 15, 1976). Hence this interference is already present in the manufacturing facility and precludes use of perchlorination. See attached copy of letter from J. Coleman Weber to Dr. I. E. Wallen.

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3834 See comments on alternate standardization procedure, line 5354.
-3835

3843 See above comments on perchlorination.
-3845

APPENDIX 1

5248 Samples collected must be representative of the personal exposure of individual workers.

5252 Records should include: Pump model & Serial no.
-5253 Sampling Tube type and no.
i.e. sampling equipment details

5258 Calibration data should also be recorded.
-5260

5266 The aim of sampling is to permit determination of the personal
-5268 exposure level primarily. This leads to a decision on compliance/
non-compliance situations. It cannot lead to the "lowest feasible
level" without other major input beyond the scope of sampling and analysis.

5273 Airflow through the pump shall be controllable within $\pm 5\%$ of the desired rate during the entire sample period.

5291 A more frequent requirement for pump calibration is required. At least monthly and preferably in the method for a daily setup calibration.

5292 Spot-checked is an open statement and means nothing.
-5293 For digital readout pumps specify parity check between expected stroke count versus actual.
For pump with rotameters specify before and after readings. We would prefer a calibration after flow stabilization and again before pump is turned off, for each sample.

5303 The sorbent tube should not be vertical.
Pointing down - loses glass wool and Florisil
Pointing up - dust from overhead, hard hat, etc. enters.
Suggest a close to horizontal location, attached to the collar of the worker.

5304 Air being sampled should pass directly into the open inlet of the sorbent tube.
This precludes filters.

5308 The recommended sample volume for this method is 50 liters (U.S. spelling)

5310 The sorbent tubes should be labelled. At this point it should reiterate checking label and I.D. Number.

5320 A bulk air sample is of no value unless the restraints required to obtain a good and recoverable sample are fully documented.

DSW 019381

- 5324 Throughout Appendix II nomenclature for PCB and PCBs is confused. In general, PCBs should be used as a noun describing a PCB mixture, while PCB is an adjective.
- 5346 This reads more smoothly if written, "This would correspond to a detection limit of 40 ng ⁱⁿ of 5 ml of desorbent".
- 5354 This alternate standardization procedure is of highly questionable utility. As pointed out in line 5358, it has not been evaluated in NIOSH laboratories. As correctly stated in the draft, the reason an alternate procedure is needed are two-fold. First, most of the GC peaks in a chromatogram of a PCB product contain more than one component. Secondly, electron capture detector response differs significantly for different PCB isomers (See Table I of the draft). These two factors indicate that the absolute quantity of PCB represented by a given peak containing unresolved components varies depending on the relative amounts of the components.

The relative composition of a given peak can vary for the following reasons:

1. PCBs with a given degree of chlorination (i.e. 42%) from different manufacturers contain different isomer ratios.
2. Component ratios vary for products with different degrees of chlorination. For example, from Table XII - 6, the ratio of dichloro- to trichlorobiphenyls for the peak with RRT 28 in Aroclor 1221 is 85:15. From Table XII - 8, the same peak in Aroclor 1242 has a ratio of 25:75. Similarly, for peak RRT 70 in Aroclor 1242 and 1254, the tetrachloro-to pentachlorobiphenyl ratios are 90:10 and 25:75.
3. Vapor pressure differences alter the composition of vaporized PCBs relative to the liquid. (See attached figure showing chromatograms of liquid and vapors from Aroclor 1016).
4. Interfering components may be present which distort the sample chromatogram. This is likely to be a major problem in capacitor and transformer manufacturing facilities because several of the PCB replacement products (i.e. phthalate esters and chlorobutyl-diphenyl ether) have similar GC retention times to PCBs and give an electron capture response.

The weight factor technique of Webb and McCall does not adequately account for these difficulties.

For those situations where the sample chromatogram closely matches the chromatogram of a reference PCB mixture, the Standard Analysis described in 5554 ff should be followed. However, if the chromatograms do not match, we believe the only satisfactory analytical method which will yield accurate results is gas chromatography/mass spectrometry (GC/MS) using selected ion monitoring (SIM). The detection limit of this technique for Aroclor 1016 is about one nanogram of PCB injected into the instrument. Considering the environmental limit of 0.05 mg/m³ recommended in this document, it might be possible to reach this lower detection limit for the total procedure by sampling as outlined in the draft, evaporating the hexane desorbent and analyzing the concentrate by GC/MS.

Alternatively, thermal desorption from a suitable solid sorbent directly into the GC/MS can be used. This well documented technique analyses the entire collected sample at once, rather than only an aliquot at a time. Response factors vary only slightly for different PCB isomers and most interferences are eliminated.

- 5381 The bulk sample must not be shipped in the same container as the sample tubes.
- 5396 The volume of air sampled can be measured to within at least $\pm 5\%$. Delete next sentence.
- 5410 Delete 100% and conclude sentence with "... recovered with a relative standard deviation of 4.4% for 27 spiked samples". Delete next sentence.
- 5460 Type of electron capture detector is not important.
- 5515 rinsing with pesticide grade acetone and hexane should follow the water rinses.
- 5533 Argon/methane is also a suitable GC carrier gas. The flow rate for either carrier gas should be only about 30 ml/min for a 2 mm id column.
- 5590 Actual retention times should be used in calculations if available. If not available, then the measurements described here can be used.
- 6118 The vapor pressures in Table XIII - 5 appear to be too high. What is the source of these data, and has their accuracy been verified?

HMB
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December 20, 1976

Dr. Jerry M. Johnson
Acting Chief,
Criteria Documentation, Section 1
NIOSH, DCDS, RM 142
4676 Columbia Parkway
Cincinnati, Ohio 45226

Dear Dr. Johnson:

At the review meeting held on November 30 on the draft criteria document for polychlorinated biphenyls I was left with the impression that future drafts of the document would continue to contain allegations that PCBs are human carcinogens and that they should be labeled as "cancer suspect agents".

In previous opportunities to comment I have emphasized the lack of persuasive evidence to provide a sound basis for designating PCBs as carcinogens. At the review meeting Dr. Paul E. Brubaker reported that the cohort in the ongoing Mobil Epidemiological Study has been reidentified and changed and that the results are now expected to differ from those initially reported. The reports, from Industrial Biostat Laboratories and the Eppley Institute, which I gave to Mr. John Fajen, contain conclusions which differ from those reached by Dr. Renate Kimbrough in her studies with female rats.

It is our considered opinion that this information further emphasizes the uncertainty of some of the available data and we strongly recommend that your office reconsider its decision to continue to designate PCBs as cancer suspect agents.

Sincerely,

ORIGINAL SIGNED BY
W. B. PAPAGEORGE

W. B. Papageorge
Manager,
Product Acceptability

ja

cc: Mr. John Fajen - NIOSH

DSW 019384

bcc: R. A. Stohr/J. C. Weber

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