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Summary Report
NIOSH-EPA
Interagency Agreement for the
Assessment of Human Health Effects
From Exposure to
Di-2-(Ethylhexyl) Phthalate

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INTRODUCTION

The National Institute for Occupational Safety and Health (NIOSH), Division of Surveillance, Hazard Evaluations and Field Studies (DSHEFS), Industrywide Studies Branch (IWSB) entered into an interagency agreement (IAG) with the Environmental Protection Agency (EPA), Health and Environmental Review Division (HERD), Epidemiology Branch in December, 1981, to assess the feasibility of conducting a retrospective cohort mortality study for occupational exposure to di-2-(ethylhexyl) phthalate (DEHP). The IAG was prompted by the results of a 2-year animal bioassay of DEHP completed by the National Cancer Institute (NCI) in 1980¹ under the National Toxicology Program. The bioassay indicated DEHP to be carcinogenic in rats and mice of both sexes at all dose levels tested and therefore was considered a potential human carcinogen.

Due to this potential human carcinogenicity, the fact that 400 million pounds of DEHP are utilized in U.S. industries annually,² and the absence of previous human health effect research, IWSB and HERD joined in an effort to conduct the feasibility study. The study was initially intended to accomplish two goals: 1) the documentation of occupational exposure levels of DEHP; and 2) the identification of a worker population suitable for a retrospective cohort mortality study.

STUDY APPROACH

The NIOSH/EPA IAG stated that the study would be approached in the following sequence:

1. information collection,
2. industrial hygiene survey/personnel record assessments, and
3. identification of a mortality study population.

Information collection consisted of conducting literature searches for: any previous industrial hygiene or epidemiology studies, industrial hygiene field monitoring procedures, and industrial application with potential for occupational exposure.

Industrial hygiene survey/personnel record assessments were performed to characterize occupational exposure levels and evaluate personnel record content for suitability for a mortality study,

The location of a suitable worker population for conducting a retrospective cohort mortality study was the ultimate objective of the NIOSH/EPA IAG. DSHEFS epidemiologists were consulted to determine the basic requirements for this study population. In general, the criteria required that a sufficiently large worker population (cohort) be identified, where there has been exposure to DEHP with minimal confounding exposures and where enough of the population was first employed a sufficient number of years ago so that

an excess in mortality can be detected if it truly exists. Also, there must be an adequate personnel record system existing to confirm the durations of employee exposure.

DISCUSSION OF STUDY POPULATION SEARCH

There was a lengthy search conducted for a worker population which met the study criteria. This search involved contacts with many companies of the type that would potentially have such a work force, meetings and contacts with appropriate trade associations and unions, and discussions with other industrial hygienists and public agencies having some research background in DEHP monitoring or study.

It became evident during the information collection that a study population without a history of confounding exposures to other toxic agents would be difficult to locate. This multiple agent exposure situation became a significant study problem since exposure to multiple agents was present throughout the polyvinylchloride (PVC) plastic processing and fabricating industries which consume 90% of the DEHP commercially utilized in the U.S.²

The problems with finding a suitable study cohort in the plastics industry resulted in a decision to seek and include other commercial categories of DEHP use. Ideally, these were to be uses without confounding exposures for a sufficient time period and at an exposure concentration level for which an influence on specific causes of mortality among exposed workers could reasonably be detected if present. Further research found two commercial areas with the potential to meet these requirements. These were high efficiency particulate air filter (HEPA) testing with polydispersed DEHP aerosol, which is generated in the respirable particle size range (0.3 to 0.5 um diameter), and DEHP manufacturing. However, after several months of searching, it became evident that it may not be possible to find any cohort meeting the established criteria.

There were two basic reasons for this situation. First, the plastics processing industry, which consumes 90% of the DEHP commercially utilized in the U.S.,² presented several problems preventing location of a suitable cohort; and second, it was not possible to locate a large enough work force in the manufacturing or aerosol filter testing areas to meet the criteria.

The plastics processing industry did have facilities with sufficient numbers of employees, but other problems made it undesirable for the study. These problems included the following:

- The PVC base resins contain a variety of chemical compounds used as fillers, coloring agents, softeners (plasticizers), stabilizers, release agents, and other processing aids. To illustrate, a laboratory identification of the volatiles from a PVC sheet heated to process temperatures indicated the presence of benzene, alkenes, and chlorinated hydrocarbons.³ Consequently, it would be very difficult to relate any employee health effects to one chemical agent.

- Processors use a variety of plasticizers in their formulations depending on the properties they wish to impart. DEHP is used as a plasticizer and is considered interchangeable with several chemically similar phthalates such as diisononylphthalate and 1,4-octylteraphthalate. Moreover, plastics processors did not know precisely when, or for how long, DEHP had been used at their facilities.
- Several companies have substituted other phthalate plasticizers due to the recent concerns about DEHP.
- Precise records of the exact daily formulations used were usually not kept. Consequently, DEHP exposure durations could not be determined.
- The major potential DEHP exposure source in PVC plastic processing is in the compounding and formulating steps where the DEHP is added to the plastic resin usually under heated conditions. However, this usually takes place in an enclosed, automated system which results in low exposure levels.

It was determined to be infeasible to locate a work force meeting the study criteria for a cohort mortality study. Therefore, it was decided to focus our efforts on characterization of worker exposure levels. Facilities were selected from the manufacturing, plastics, and filter-testing areas suitable for industrial hygiene evaluations, and surveys were conducted in order to characterize worker exposure levels.

INDUSTRIAL HYGIENE SURVEY PROTOCOL

Prior to conducting in-plant investigations it is the policy of IWSB to prepare a survey protocol. The protocol details events that will occur during the survey, the type of information required from the company, and the sampling methods, equipment, and analysis techniques that will be employed.

Preparation of the DEHP IAG survey protocol involved addressing a problem unique to this study. This was the fact that DEHP may be present as a plasticizer in some sampling train components such as tubing, pump casings, and analytical labware such as glassware draining racks, and floor tiles. This could potentially cause sample or analyte background contamination with DEHP.

To address the possible DEHP contamination of the field samples by the sampling train, it was tested for DEHP generation. The testing was accomplished by placing a complete sampling train, including sampling media, in an enclosed chamber without an outside air source. The sampling pump was operated for 48 hours within the chamber. This procedure was repeated with five different sampling train set-ups, and the sampling media was analyzed for the presence of DEHP. Also, the sampling media cassette holders were tested by placing five cassette/media set-ups in a low temperature oven for 8 hours at temperatures ranging from 80 to 150°F and having the filter media analyzed for DEHP. No DEHP was detected in the samples for each test.

Concerning the possibility of analytical laboratory background contamination the following precautions were taken. Spiked samples of a known DEHP concentration were prepared by the NIOSH quality control laboratory and two were submitted as normal field samples to the NIOSH contracted analytical lab (Utah Biomedical Test Laboratories) with each field sample set. Also, six sampling media blanks were submitted with each survey sample set, two of which were falsely labeled as actual field samples as an extra QA check. Furthermore, the contract lab adhered to NIOSH laboratory quality control procedures of which one aspect was to run laboratory blanks each day during the analysis to determine the laboratory DEHP background levels.

The following in-plant DEHP survey procedure was then prepared.

1. Hold an opening conference with appropriate plant personnel to explain the nature and purpose of the investigation.
2. Upon completion of opening conference proceed with a guided tour of the plant areas where DEHP is involved.
3. Following guided tour conduct area/personal environmental sampling for DEHP for the remainder of the work shift. Sampling of an additional shift will be requested if all DEHP process areas of concern can not be covered in the first one.
4. During environmental monitoring period meet with plant representative to obtain information pertinent to the study criteria.

SAMPLING TRAIN - Environmental sampling was performed with Dupont Model P-2500 personal sampling pumps at a flow rate of 2.5 liters per minute (Lpm). The sampling media was Millipore AA 37-mm diameter, 0.8-um pore size, mixed-cellulose ester filters. The filters were contained in styrene cassettes using a support pad and connected to the pump with 1/4" ID gum rubber tubing.

SAMPLING STRATEGY - The environmental monitoring plan was to collect a minimum of two area samples as near as possible to the points of highest probable air concentration of DEHP, four general area samples in DEHP process areas and two personal breathing zone samples in each area if appropriate.

SAMPLE ANALYSIS - The filters were analyzed by gas chromatography using NIOSH analytical method S-40⁴ with some modification of the desorption process, gas chromatograph, column, oven conditions, and carrier gas. The samples were desorbed for 1 hour in 1.5 mL of carbon disulfide containing 1 uL/mL hexadecane as an internal standard. The gas chromatograph was a Hewlett-Packard Model 5731 equipped with a flame ionization detector utilizing a column of 12m x 0.21 mm ID fused silica capillary with an inner coating of 0.25 um Se-30. The oven was at 230°C isothermal, and helium was used as the carrier gas in a split mode of operation with a split ratio of 10 to 1. The DEHP detection limit was 0.01 mg/sample.

SELECTION OF FACILITIES FOR FIELD STUDY

The process of selecting facilities for field study began by reviewing the information obtained from literature searches. This information was used to determine which types of facilities were the largest producers/users of DEHP. The Standard Industrial Classification code (SIC) for the types of facilities selected were obtained from the SIC manual.⁵ The SIC codes were then used to obtain company names from the Dunn and Bradstreet Million Dollar Directory.⁶

Companies were contacted regarding annual DEHP consumption/production, types of processes where DEHP is used, as well as the size of and length of time DEHP has been used for any potentially exposed work force.

While compiling this information a meeting was held with the Chemical Manufacturers Association (CMA) to inform them of the study and request information regarding commercial production and uses of DEHP. The CMA provided information for the largest U.S. manufacturers and a list of the Top 400 Plastics Processing Plants. The CMA stressed the importance of effective quality assurance procedures because of the many confounding agents present in the plastics industry and possible background contamination encountered in analytical labs. The CMA also pointed out that it would be very difficult to link any health effects to a specific agent in the plastics industry due to the multiple compounds that are used in their formulations, and the fact that the ratios and types of specific compounds used are changed frequently. The CMA suggested that the Society of The Plastics Industry (SPI) was a trade association that may provide further information of DEHP use in the plastics processing industry.

Contact with the SPI yielded some more specific information about the use of DEHP in the plastics industry. The SPI said the major consumption of DEHP in plastics formulations was as a plasticizer in PVC products, and mainly in PVC sheet or film material. They also indicated the highest potential source of worker exposure in these processes would be during the compounding and formulating of the plastic resin since the DEHP is blended in there, and this stage often involves heating.

Considering the presence of complex multiple agent exposure in the plastics industry, the decision was made to devote the majority of field survey efforts to manufacturing and aerosol filter testing operations, which did not present this problem. Facilities selected for study included a manufacturer, two aerosol filter testers, and a PVC plastic sheet processing facility.

DISCUSSION OF FIELD STUDY RESULTS

The DEHP air level concentration results for the industrial hygiene field samples are presented in Tables I - IV. A sampling flow rate of 2.5 Lpm was used rather than the 1 Lpm recommended by NIOSH method S-40⁴ because it was anticipated that submilligram levels may be present, and therefore a

higher flow rate, would be needed to get a detectable amount of DEHP. This modification was discussed with the NIOSH Division of Physical Sciences and Engineering, Monitoring and Control Research Branch, Quality Assurance Section. The Quality Assurance Section confirmed that using the 2.5 Lpm flow rate would present no analytical problems.

The monitoring data in Tables I - IV show that the DEHP personal worker exposure ranged from non-detectable (ND) to 0.29 milligrams of DEHP per cubic meter of sampled air (mg/m^3). These levels are at least an order of magnitude below the OSHA 8-hour Permissible Exposure Limit⁷ (PEL) of 5 mg/m^3 . Also, except in extreme worst-case situations where samples were collected within a few inches of a source, the area samples ranged from ND to 0.26 mg/m^3 . The area sample shown in Table III, which had a concentration of 1.38 mg/m^3 , was collected in an aerosol exhausting hood and was not intended to be representative of a potential worker exposure. Likewise the area sample shown in Table IV, taken at an extrusion heating screen, had an air concentration of 4.23 mg/m^3 of DEHP, but was not representative of employee exposure.

The data for the manufacturing facility in Table I show that all personal employee exposure levels were below the analytical limit of detection. Similarly, only two area samples, which were collected at locations where the process was occasionally opened to outside air, had detectable levels of DEHP. These area samples are not considered to be representative of employee exposure. This is confirmed by the ND exposures for the process operators who were occasionally in these areas. These consistently ND DEHP air levels throughout the manufacturing process are probably best explained by the fact that it is an enclosed process with only occasional brief exposure to outside air.

Tables II and III show that the personal employee exposure levels for the aerosol filter testing facilities ranged from 0.01 to 0.14 mg/m^3 of DEHP, and the area levels from ND to 1.38 mg/m^3 . Again, the exposure levels are well below the 5 mg/m^3 OSHA PEL.⁷ The area sample shown in Table III taken in the exhaust hood of a filter-testing manifold had a DEHP level of 1.38 mg/m^3 , but is not representative of personal exposure. This is confirmed by the tester operators' personal exposure level of 0.07 mg/m^3 and the operator helpers' exposure of 0.14 mg/m^3 .

The personal and area DEHP exposure levels shown in Table IV for the PVC sheet process seem to be slightly higher than for the manufacturing and filter testing operations. The area sample collected within a few inches of the extruding/heating screen had a DEHP concentration of 4.23 mg/m^3 . This was the highest level seen for all surveys, but again was not an indicator of actual potential worker exposure. This is shown by the personal exposures found for the process operators which ranged from 0.06 to 0.29 mg/m^3 of DEHP.

Overall, the data in Tables I - IV shows that the potential employee DEHP exposures in all three processes were at least an order of magnitude below the current OSHA TWA exposure standard of 5 mg/m^3 .

CONCLUSIONS

The plastics processing industry uses about 90% of the total DEHP used in the U.S., and the PVC plastics processors use the majority of that 90%. However, based on the reasons previously described, it does not seem possible to locate a suitable study population, or to relate any worker health effects found to DEHP specifically. Therefore, it is concluded that the plastics processing industry would not be feasible for an epidemiologic study.

The DEHP manufacturing and aerosol filter testing areas do offer worker populations without the complex multiple agent exposure found with plastics but the populations are too small (<25) and not exposed long enough (<20 years). Consequently, these areas do not seem to offer a suitable study cohort.

Furthermore, the field monitoring conducted for the three industries indicates that worker exposure levels are consistently less than 0.5 mg/m^3 , an order of magnitude below the current OSHA TWA standard of 5 mg/m^3 .

Therefore, due to the lack of a suitable study cohort and the existing low levels of exposure it is recommended that a retrospective mortality study not be pursued at this time.

FURTHER ONGOING RESEARCH

Currently there are bio-research projects underway intended to provide information for the actual human biological effects from DEHP exposure. The National Institute of Environmental Health Sciences (NIEHS) is conducting a study to compare the toxic mechanism of DEHP in rodents with that in humans. Also, the CMA is sponsoring a research effort to compare the metabolism of DEHP by rodents with that of primates.

REFERENCES

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Table I
 DEHP Exposure Levels
 at a Manufacturing Facility
 January 26 - 27, 1982*

Sample Location/Description	Sampling Time (min.) ⁺	Sample Volume (L)	DEHP Conc. (mg/m ³)
Personal on Process Operator	262	655	ND ^t
Area in Control Room	282	705	ND
Personal on Process Operator	278	695	ND
Worst-Case Near Process Sample Port	274	685	0.16
Personal on Process Supervisor	280	700	ND
Personal on Process Operator	276	690	ND
Area in Control Lab	274	686	ND
Personal on Truck Loader	279	698	ND
Personal on Control Room Operator	281	702	ND
Worst-Case Area Near Carbon Filter Drop Shute	277	693	0.15
Personal on Plant Maintenance Man	276	690	ND
Personal on Plant Maintenance Man	280	701	ND

* Sample concentrations are reported based on TWA for period of time sampled.

+ Sample pumps were calibrated to a flow rate of 2.5 Lpm.

t DEHP was not detected at the 0.01 mg/sample detection limit.

Table II
 DEHP Exposure Levels
 at an Aerosol Filter Testing Facility
 June 28, 1982*

Sample Location/Description	Sampling Time (min.) ⁺	Sample Volume (L)	DEHP Conc. (mg/m ³)
Personal on Q-127 Operator Testing Gas-Mask Filters	282	705	0.01
Worst-Case Area Sample Near Testing Manifold of Above Unit	278	695	0.03
Worst-Case Area Sample Near Testing Manifold of Above Unit	273	683	0.03
Worst-Case Area Sample Near Testing Manifold of Q-127 Commercial HEPA Testing Unit	250	625	0.05
Personal on M-14 Operator Testing Gas Masks	275	688	0.12
Worst-Case Area Sample Near Testing Face of Above Unit	289	723	0.15
General Area of M-17A-1 Assembly Line	272	680	0.03

* Sample concentrations are reported based on TWA for period of time sampled.
 + Sample pumps were calibrated to a flow rate of 2.5 Lpm.

Table III
 DEHP Exposure Levels
 at an Aerosol Filter Testing Facility
 July 27, 1982*

Sample Location/Description	Sampling Time (min.) ⁺	Sample Volume (L)	DEHP Conc. (mg/m ³)
Personal on Filter Testing Operator	269	673	0.07
Personal on Testing Operator Helper	265	663	0.14
Worst-Case In Exhaust Hood Above Filter Testing Manifold	267	668	1.38
Area on Operator Control Panel	264	660	0.05
Area on Operator Helpers' Bench	250	625	0.10
General Plant Area	247	618	ND ^t
General Plant Area	243	608	0.03

* Sample concentrations are reported based on TWA for period of time sampled.

+ Sample pumps were calibrated to a flow rate of 2.5 Lpm.

t DEHP was not detected at the 0.01 mg/sample detection limit.

Table IV
 DEHP Exposure Levels
 at a PVC Plastics Processing Facility
 October 20, 1982*

Sample Location/Description	Sampling Time (min.) ⁺	Sample Volume (L)	DEHP Conc. (mg/m ³)
Area Next to Banbury Mixing Unit	232	580	0.12
Personal on Compounder	258	645	0.06
Personal on Feed Operator	247	618	0.29
Area Next to Feed Mill	246	615	0.16
Worst-Case Area Next to Extruding /Heating Screen Outlet Conveyor	246	615	4.23
Personal on Calender Utility Man	253	633	0.09
Area above Calenders	246	615	0.11
Area Near Calendering Entrance	249	623	0.26
General Area 20 Feet Away From Processing Line	237	593	ND ^t

* Sample concentrations are reported based on TWA for period of time sampled.

+ Sample pumps were calibrated to a flow rate of 2.5 Lpm.

t DEHP was not detected at the 0.01 mg/sample detection limit.

Appendix I
Companies Considered for DEHP Industrial Hygiene Survey

Company Name	Type of DEHP Use	Date DEHP First Used	Date DEHP Use Stopped	Amount of DEHP Used (lb/yr)	# of Workers Potentially Exposed
General Tire & Rubber Co.	Tire Plasticizer	*	*	*	1
Belden Corp.	Plasticizer & Wire Castings	*	*	600,000	3
Gates Rubber Co.	Rubber Hose				
	Plastisizer	Early 1960	Still Used	340,000	6
Cambridge Filter Co.	HEPA Filter Testing	1953	Still Used	6,800	10
Conoco Chem.	Manufacture & PVC Resin Compounding	*	Still Used	*	12
Millipore Corp.	HEPA Filter Testing	*	Still Used	15	1
Occidental Petro. Corp.	Calandering	*	Still Used	*	5
Diamond Shamrock Corp.	Molding	1976	Still Used	*	6
Velcon Filter Corp.	None	NA	NA	NA	NA
Pall Corp.	HEPA Filter Testing	*	Still Used	15	2
MSA Co.	HEPA Filter Testing	1960	Still Used	1,400	26
Cambridge Filter Co.	HEPA Filter Testing	1853	Still Used	6,100	20
Tenneco Chem.	+	*	NA	NA	NA
Reynolds Metals	+	*	NA	NA	NA
Shelton Globe Corp.	+	*	NA	NA	NA
Goodyear Tire & Rubber	+	*	NA	NA	NA
Abbot Labs	HEPA Filter Testing	1972	Still Used	10	3
Travenol Labs	Plastic Extrusion	*	Still Used	*	5
Badische Corp.	Manufacture	1971	Still Produced	Production of 66 million	10

* Information not provided by company

+ DEHP was used in the past but use was discontinued.

