2,3,7,8-TCDD in human blood

Henderson and Patterson (1988) investigated the distribution of [\(^3\)H]2,3,7,8-TCDD in human whole blood and its association with lipoproteins. They found that [\(^3\)H]2,3,7,8-TCDD was associated entirely with the red cell free phase and that >80% was associated with lipoproteins. The distribution of \([\text{\[^3\]H}]2,3,7,8-\text{TCDD}\) among lipoprotein fractions from three fasting, normolipemic donors found 55, 17 and 27% of the compound associated with LDL, VLDL and HDL fractions, respectively. The authors indicated that since 2,3,7,8-TCDD in blood favors the lipoprotein vehicle, the cellular lipoprotein receptors, especially LDL receptors, may be important in the uptake and subsequent cellular effects of 2,3,7,8-TCDD.

Recently, Patterson, et al. (1987) developed a high-resolution gas chromatographic/high-resolution mass spectrometric analysis for 2,3,7,8-TCDD in human serum. The arithmetic mean of the individual human serum samples was 47.9 ppq on a whole-weight basis and 7.6 ppt on a lipid weight basis. Paired human serum and adipose tissue levels of 2,3,7,8-TCDD have been compared by Patterson, et al. (1988) and Kahn, et al. (1988). Both laboratories reported a high correlation between adipose tissue and serum 2,3,7,8-TCDD levels when the samples were adjusted for total lipid content. This correlation indicates that serum 2,3,7,8-TCDD is a valid measurement of 2,3,7,8-TCDD body burden concentration.

A lack of correlation between estimated exposure to 2,3,7,8-TCDD and sera levels of 2,3,7,8-TCDD was reported in a preliminary report in the MMWR (1987) which compared Vietnam veterans with
military histories indicating exposure to herbicides containing 2,3,7,8-TCDD and non-Vietnam veterans with presumably no unusual exposure to 2,3,7,8-TCDD. At least in these preliminary results there was no difference in the range of 2,3,7,8-TCDD levels (1-9 ppt based on lipid weight) or the median 2,3,7,8-TCDD level (3.9 ppt for the presumably exposed group and 3.8 ppt for the non-exposed group). The completed CDC Veterans Health Study (1988) assessed serum levels of 2,3,7,8-TCDD in 646 ground combat troops who served in Vietnam and in 97 veterans who did not serve in Vietnam. The serum 2,3,7,8-TCDD levels in Vietnam veterans was 4.2 ± 2.6 (mean ± S.D.) ppt on a lipid weight basis and 4.1 ± 2.3 ppt for non-Vietnam veterans. Only two men, both Vietnam veterans, had clearly elevated levels (>20 ppt). The authors of the study suggest that most U.S. Army ground troops who served in Vietnam were not heavily exposed to 2,3,7,8-TCDD, with the possible exception of men involved in handling herbicides, but, as stated earlier, this study has been criticized by scientists who were at one time involved with it. In a study of potentially heavily exposed Vietnam veterans, MMWR (1988) reported on an Air Force study of Ranch Hand veterans who were either herbicide loaders or herbicide specialists in Vietnam. The mean serum 2,3,7,8-TCDD level of 147 Ranch Hand personnel was 49 ppt, based on total lipid-weight, while the mean serum level of the 49 controls was 5 ppt. Additionally, 79% of the Ranch Hand personnel and 2% of the controls had 2,3,7,8-TCDD levels ≥10 ppt. The distribution of 2,3,7,8-TCDD levels in this phase of the Air Force health study
indicates that some Ranch Hand personnel had unusually heavy 2,3,7,8-TCDD exposure. This report also estimated the half-life of 2,3,7,8-TCDD in humans to be ~7 years on the basis of 2,3,7,8-TCDD levels in serum samples taken in 1982 and 1987 from 36 of the Ranch Hand personnel who had 2,3,7,8-TCDD levels >10 ppt in 1987. Similar results were obtained by another laboratory, which compared 2,3,7,8-TCDD levels in blood and adipose tissue of Agent Orange-exposed Vietnam veterans and matched controls (Kahn, et al., 1988). This study also examined heavily exposed Vietnam veterans who handled herbicides regularly while in Vietnam. Vietnam veterans who were heavily exposed to Agent Orange exceeded matched control subjects in both blood and adipose tissue levels of 2,3,7,8-TCDD but not in the levels of the 12 other 2,3,7,8- substituted dioxins and dibenzofurans that were detected. Since only 2,3,7,8-TCDD among these compounds was present in Agent Orange but all are present in the population of the industrialized world, it is likely that the elevated 2,3,7,8-TCDD levels arose from wartime exposure. Although this study may be able to distinguish heavily exposed men from others, the data do not address the question of identifying persons whose exposures are moderate and who may constitute the bulk of the population, both military and civilian, who have been exposed to greater than background levels of 2,3,7,8-TCDD.

**Excretion of 2,3,7,8-TCDD in Humans**

Poiger and Schlatter (1986) investigated the excretion of 2,3,7,8-TCDD in a 42-year old man after injection of 105 ng [\(^3\)H]-2,3,7,8-TCDD in 6 ml corn oil. The half-life for elimination was
estimated to be 2120 days. In another study, the half-life of 2,3,7,8-TCDD in humans was estimated to be 7 years on the basis of 2,3,7,8-TCDD levels in serum samples taken in 1982 and 1987 from 36 of the ranch hand personnel who had 2,3,7,8-TCDD levels >10 ppt in 1987 (MMWR, 1988). In a subsequent report, Pirkle, et al., (1989) reported that the median half-life of 2,3,7,8-TCDD in these Ranch Hand veterans was 7.1 years (95% confidence interval about the median of 5.8 - 9.6 years), however, this study also shows that serum dioxin testing is unreliable 16% of the time and that dioxin in humans has a potentially wide range for half-life, which, at the low end, would bring subjects down to background in relatively short periods. These studies indicate that 2,3,7,8-TCDD is exceedingly persistent in humans.

The caveat in the use of any of this data, due to problems with test reliability and sensitivity, and half-life variability, is that, although the presence of elevated 2,3,7,8-TCDD in tissue, serum or excreta indicates exposure, its absence does not necessarily indicate lack of exposure.

**CONCLUSIONS**

This review of the scientific literature leads to the following conclusions:

1. There is a significant statistical association between exposure to phenoxyacetic acid herbicides and/or their associated contaminants (chlorinated dioxins) and non-Hodgkin's lymphoma, soft tissue sarcoma, skin disorders/chloracne, subclinical hepatotoxic
effects (including secondary coproporphyrinuria and chronic hepatic porphyria), and porphyria cutanea tarda (most likely only in individuals with inherited uroporphyrinogen decarboxylase deficiency). The aggregate interpretation of several sound studies showing a statistically significant association for each of these conditions makes this conclusion inescapable.

(2) The scientific evidence supporting the existence of a significant statistical association between exposure to phenoxyacetic acid herbicides and/or their associated contaminants (chlorinated dioxins) is at least as strong as the scientific evidence of a lack of the association for the following adverse health effects: Hodgkin’s disease, neurologic effects, and reproductive and developmental effects. For each of these health effects, there are sound scientific studies showing statistical significance and strong scientific evidence of an association between exposure and effect. However, a statistically significant association is not as consistently supported for these effects as for the first group of health effects.

(3) The above eight adverse health effects satisfy the VA’s test for an association which qualifies for disability compensation, i.e., where the scientific evidence shows that a significant statistical association is "at least as likely as not." 38 C.F.R. § 1.17(d)(1).

(4) There are other adverse health effects for which there is sound scientific evidence of an association with exposure, but the evidence does not reach the level of formal statistical
significance. The limited data available at this time show an association, but not a significant statistical association, between exposure to phenoxyacetic acid herbicides and/or dioxin and the following diseases: leukemias, cancers of the kidney, testis, pancreas, stomach, prostate, colon, hepatobiliary tract, and brain, psychosocial effects, immunological abnormalities, gastrointestinal ulcer, and altered lipid metabolism. Further research should be directed at these associations, and policy-makers, cognizant of the limitations on finding significant statistical associations and of the obligation to give the veteran the benefit of the doubt, would be justified in viewing these disorders in a more conclusive light for the purpose of establishing entitlement to disability compensation.

(5) The epidemiologic evidence on the associations between exposure and the adverse health effects described above is strongly supported by a wide range of experimental animal studies.

SELECTED SECONDARY CONCLUSIONS

(1) Contrary to the contention of the authors, the CDC Selected Cancers Study may provide additional support to the evidence that exposure to Agent Orange in Vietnam caused an increased risk of non-Hodgkin's lymphoma.

(2) The exposure index used in the Air Force's Ranch Hand Study is not a good measure of actual dioxin exposure, and statistically significant individual findings are not possible because of the small size of the group under study. Statistically
significant group differences with a harmful impact on Ranch Hand veterans have been detected in several health areas, including: all cancers combined, both verified and suspected; skin cancers alone; hereditary and degenerative neurological diseases; coordination abnormalities; psychological and sleep disorders; certain dermatologic disorders; pulse irregularities; increase in thyroid stimulating hormone; among black Ranch Hands, higher mean counts for "natural killer cells" as compared to blacks in the control group; and among Ranch Hands who are heavy smokers, more abnormal composite skin reactions as compared to heavy smokers in the control group.

(3) Although the presence of elevated 2,3,7,8-TCDD in tissue, serum or excreta indicates dioxin exposure, its absence does not necessarily indicate a lack of exposure because of problems with test reliability and sensitivity, and half-life variability.
APPENDIX A

ILLUSTRATIVE STATEMENTS IN THE LITERATURE ON THE SCIENTIFIC VALIDITY OF EXTRAPOLATION OF EXPERIMENTAL ANIMAL CARCINOGENICITY DATA TO HUMAN CANCER RISK


"Any substance which is shown conclusively to cause cancers in animals, when tested under (adequate) conditions, should be considered potentially carcinogenic for man --."


"Any substance which is shown conclusively to cause tumors in animals should be considered carcinogenic and therefore a potential cancer hazard for man. Exceptions should be considered only where the carcinogenic effect is clearly shown to result from physical, rather than chemical, induction, or where the route of administration is shown to be grossly inappropriate in terms of conceivable human exposure."


"Ordinarily, if a substance has produced positive results in a single adequately designed and conducted animal bioassay and no other data are available, the conclusion is that the substance is likely to pose a risk of cancer to humans. --Further confirmation that the substance poses a carcinogenic hazard to humans is obtained from bioassay data showing reproducibility of results, positive dose-response relationships and concordance of results."

"Moreover, negative epidemiologic data, questionable because of limitations in the power of detection of such studies, do not deny the conclusion of carcinogenicity on the basis of animal bioassays."

Based on detailed, testimony from a wide range of recognized scientific authorities, and on an extensively documented record, OSHA concluded as follows:

"The validity of qualitatively extrapolating animal test results to humans is firmly based upon substantial and empirical evidence in the Record, --. Not only have experiments in test mammalian animals given positive carcinogenic test results for every compound known to cause cancer in humans, except arsenic and perhaps benzene, but although there may be wide variations in the susceptibility of various species to cancer, evidence indicates that a substance that causes cancer in one mammalian animal species is likely to do so in most other mammalian species tested. Substantial evidence and scientific data in the Record indicate, in sum, that laboratory animals are suitable test models for determining the cancer-causing potential of a toxic substance to humans."

"OSHA concludes that the general principle that substances shown to be carcinogenic in test animals should be presumed to pose a qualitative carcinogenic hazard to exposed humans was overwhelmingly supported, except as so qualified below (in relation to the adequacy of the carcinogenicity test); indeed, the specific scientific documentation for the principle is steadily being enlarged."

"Retrospective epidemiologic studies of exposed workers are very difficult to carry out in a systematic and unbiased manner, and in fact comparatively few good studies have been reported."

"Epidemiologic studies are complicated by many factors, including the selection of exposed and control groups, definition and measurement of exposure, length of exposure and follow-up periods, and various kinds of bias."

"Non-positive" epidemiologic studies cannot, in principle, establish the safety of agents under suspicion on other grounds. None of the studies presented as 'non-positive' in this rulemaking (including those on DDT, Aldrin/Dieldrin, Chlordane/Heptachlor, Phenobarbital, 3,3-Dichlorobenzidine, Isoniazid, 2,4-Dinitrotoluene, Fibrous Glass and Saccharin) stands up to critical scrutiny."


"Properly designed and conducted tests using appropriate animal species are accepted valid ways to identify chemical substances that may cause cancer in humans. -- Most data for identifying potential cancer risks must come from animal studies. -- Animal tests are a scientifically sound and valid way to
identify substances that are likely to cause human cancer."

"In one study of chemicals and chemical processes, 26 substances linked to human cancers were examined. All but two produced cancer in animals (Tomatis et al, 1978). Six were first identified as animal carcinogens and only later were found to cause cancer in humans."


"Chemicals cannot be tested for carcinogenicity in humans because of ethical considerations. A substantial body of experimentally derived knowledge and the preponderance of expert opinion support the conclusion that testing of chemicals in laboratory animals provides reliable information about carcinogenicity. Animal tests employ whole mammal systems, and although they differ one from another, all mammals, including humans, share many biological features (NRC, 1977)."

"Effects in animals, properly qualified, are applicable to man. This premise underlies all of experimental biology and medicine, but because it is continually questioned with regard to human cancer, it is desirable to point out that cancer in men and animals is strikingly similar. Virtually every form of human cancer has an experimental counterpart, and every form of multicellular organism is subject to cancer, including insects, fish, and plants. Although there are differences in susceptibility between different animal species, and between individuals of the same strain, carcinogenic chemicals will affect most test species, and there are large bodies of experimental data that indicate that exposures that are carcinogenic to animals are likely to be carcinogenic to man, and vice versa."


"The validity of using animal bioassays to identify substances that pose cancer risks to humans rests upon both theoretical and empirical evidence. On the theoretical side, cancer in humans is likely to be biologically similar to cancer in other mammals (see "Oncogens", page 11); and most carcinogens are believed to act on the same basic biological systems in all mammalian species. Empirically, most substances that are carcinogenic in one animal species are also found to be carcinogenic in other animal species when adequately tested. Further, almost all substances that are known to be carcinogenic in humans, for which animal data exist, are also carcinogenic in animals. Thus, there is substantial scientific support for the assumption that a substance carcinogenic
in animals will, with high probability, be carcinogenic in humans."


"In the absence of adequate data in humans, it is reasonable for practical purposes to regard chemicals for which there is sufficient evidence of carcinogenicity in animals as if they presented a carcinogenic risk to humans."


"Positive results in properly conducted animal bioassays are considered to be predictors of qualitative response in humans (IARC, 1980; NRC, 1977, 1983; NTP, 1984; OSTP, 1985; OTA, 1981). The scientific rationale for this approach is simply that animals are the closest models to the human for cancer studies. In addition, many carcinogens produce cancer in several species, and all known human carcinogens have been shown to produce tumors in at least one animal model (NTP, 1984). Benzene and arsenic trioxide, the two former holdouts from this general rule, have now been shown to be carcinogenic in animals (Goldstein, et al., 1982; Maltoni and Scarnato, 1979; Pershagen, et al., 1984). For some chemicals (e.g., aflatoxin B1, DES, vinyl chloride, mustard gas, melphalan, and 4-aminobiphenyl), the positive results in experimental animals preceded the epidemiological evidence. The overall patterns of chemical metabolism are generally similar in humans and laboratory animals (Rall, 1979), although the rates of metabolism and the type and site of cancer may differ (IRLG, 1979; OTA, 1981). For example, the metabolism of B(a)P is qualitatively the same in all species and systems studied (Sims, 1976)."


"All policies accept the use of animal data as predictive for human beings. Explicitly or implicitly, all the policies acknowledge that substances shown to be carcinogenic in animals should be presumed to present a carcinogenic hazard to humans.

"An often-quoted statement on the value of animal data in assessing human risk is that of IARC. Their principle is based on two points: that a number of chemicals were first identified as animals carcinogens, and then evidence confirmed carcinogenicity in humans. Second, all chemicals accepted as human carcinogens that have been adequately studied in animals are positive in at least one species. IARC concluded:
Although this association cannot establish that all animal carcinogens also cause cancer in humans, nevertheless, in the absence of adequate data on humans, it is biologically plausible and prudent to regard agents for which there is sufficient evidence of carcinogenicity in experimental animals as if they presented a carcinogenic risk to humans. (IARC, 1987).


"All chemicals known to increase cancer in humans that have been studied under adequate experimental conditions, also cause cancer in laboratory animals."


Based on a detailed review of the limitations and difficulties in epidemiologic studies, Nicholson concluded:

"Considerable human data are available that would causally associate human cancer with occupational exposures through the identification of substantial workplace risks. Much additional data are available, indicating lesser risks, that have not achieved widespread acceptance because of the limitations of epidemiologic techniques. Limitations of epidemiologic techniques also limit the associations that can be made, using general population data, between cancer mortality and occupation. These same uncertainties, however, also affect assertions of absence of effect. Apparently 'negative' results must be evaluated with the same critical view as are most 'positive' results."


A National Academy of Sciences/National Research Council (NAS/NRC) panel on pesticide use (published as Contemporary Pest Control Practices and Prospects) examined the relationship between dose of various chemicals that appeared to cause cancer in humans and in laboratory animals. When the lowest carcinogenic dose in the most sensitive species was compared to that in humans for three compounds -- benzidine, chlornaphazine and cigarette smoke -- a close relationship was found. The animals were more sensitive for another three compounds: aflatoxin, diethylstilbestrol (DES), and vinyl chloride.

"In summary, of the 23 compounds or mixtures (which are carcinogenic in humans), 21 are positive in animal carcinogenicity
studies, one is questionable (azathioprine), and one has simply not been studied (treosulphan, an obscure cancer chemotherapeutic agent). In terms of site-specificity, one or more sites in the human were predicted by laboratory animals for 18 of the 23 agents, including treosulphan and azathioprine. If these two are not included since they were not tested there in laboratory animals, the sites were the same for 18 out of 21 compounds. I have grouped leukemia, lymphoma, and reticuloendothelial disease. This all suggests that animals predict fairly well for humans."

There are "-- seven compounds or groups of compounds which were discovered to be carcinogenic first in laboratory animals. Demonstration of carcinogenity in human studies came later: 4-aminobiphenyl, diethylstilbestrol, mustard gas, vinyl chloride, aflatoxins, bis(chloromethyl) ether, and melphalan."


It is fallacious to assume "-- that the existence of human data per se (independently of their quality) indicated a higher probability that the exposure was carcinogenic to humans, or even that exposures for which only experimental results are available do not represent a human health hazard. In fact, within the IARC Monographs, it is considered reasonable, for practical purposes, to regard chemicals for which there is sufficient evidence of carcinogenicity derived from experimental results, in the absence of adequate human data, as if they were carcinogenic to humans."

"There are now 119 chemicals evaluated in the Monographs for which experimental data provide sufficient evidence of carcinogenicity but for which there are absolutely no human data. The IARC Directory of Ongoing Research in Cancer Epidemiology for 1985 reports that only nine of these 119 chemicals are subjects of epidemiological surveys."

"In a study undertaken a few years ago, a similar proportion (about nine percent) of the chemicals in current commercial use in the USA, for which there is sufficient evidence of carcinogenicity in experimental animals, was found to be the object of epidemiological study or medical surveillance. -- Small numbers of exposed individuals, short durations of exposure or simultaneous exposure to such a variety of compounds as to obscure the effect of the one compound in particular, may in some instances raise insurmountable difficulties for carrying out an epidemiological study."

"Obviously, the existence of sufficient evidence of carcinogenicity in experimental tests has not exerted the same attraction for epidemiologists as for experimentalists, as
The qualitative assessment of carcinogenic risks to humans ordinarily is based on data from experiments in animals. (Guidelines for Chemical Carcinogen Risk Assessments and their Scientific Rationale, Cal. Health and Welfare Agency, Dept. of Health Services (Nov. 1985) p. C-20 [hereafter cited as California Cancer Guidelines]). It is unethical to test humans, and because of 20 to 30 year latency period of many human cancers, epidemiological studies do not adequately warn humans and protect them from the risk of exposure to new carcinogens. (Id., at p. B-10). For recognized human carcinogens, the first evidence of carcinogenicity frequently is found in test animals; only afterwards are cancer effects looked for, and found, in humans (Id., at p. B-24). Thus, the principle which supports qualitative animal to human extrapolation from carcinogenesis "has been accepted by all health and regulatory agencies and is regarded widely by scientists in industry and academia as a justifiable and necessary inference." (Rep., Office of Science and Technology Policy, 50 Fed. Reg. 10375 (March 14, 1985)).

NOTE: Although this appendix refers solely to the extrapolation to humans of animal carcinogenicity data, the same extrapolation holds for other medical effects and for the same reasons. For example, dioxin induced atrophy of the thymus gland and liver damage are seen in all species tested.
APPENDIX B

Literature Considered by the Task Force but not by the VA’s Advisory Committee


Andrews, J.S. Missouri dioxin studies; an update on long-term health effects. Dioxin ’89, Abstract # EPI07.


Erickson, J.D., Mulinare, J., McClain, P.W., Fitch, T.G., James, L.M., McClearn, A.B., and Adams, M.J. Vietnam veterans risks for fathering babies with birth defects. JAMA 252: 903 -


-52-


Huong, L.D., Phuong, N.T.N., Thuy, T.T., and Hoan, N.T.K. An
estimate of the incidence of birth defects, hydatidiform mole
and fetal death in utero between 1952 and 1985 at the
obstetrical and gynecological hospital of Ho Chi Minh City,

Hryhorczuk, D.O., Wallace, W.H., Persky, V., Furner, S., Oleske,
D.M., and Levy, P. General health status of workers who had
been engaged in the production of chlorinated phenols and
chlorphenoxy acid esters: W.G. Krummrich Study. Dioxin '89,
Abstract # EPI06.

Irey, N.S., Mullick, F.G., Foster, W.D. A morphologic study of

abnormalities 17 years after accidental exposure to 2,3,7,8-
(1988).

Johnson, E.S. Association between exposure to
phenoxy/chlorophenols and soft-tissue sarcomas and malignant
as of 11/24/89).

Johnson, F.E., Kugler, M.A., Brown, S.M. Soft tissue sarcomas and

Kahn, P.C., Gochfeld, M., Nygren, M., Hansson, M., Rappe, C.,
Velez, H., Ghent-Guenthner, T. and Wilson, W.F. Dioxins and
dibenzo[ghi]furans in blood and adipose tissue of Agent Orange-
exposed Vietnam veterans and matched controls. JAMA 252:

Evaluation of chromosomal damage in males exposed to Agent
Orange and their families. J. Craniofacial Genetics and

Kim, C.S., Keizer, R.F., Pritchard, J.B. 2,4-Dichlorophenoxyacetic
acid intoxication increases its accumulation within the brain.


Klawans, H.L., Wilson, R.S. and Garron, D.C. Neurologic problems
following exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin
(TCDD, Dioxin) in Neurotoxins and their pharmacological

-54-


MMWR. Preliminary report: 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure to humans - Seveso, Italy. MMWR/CDC 37: 733 - 736 (1988).

Mohammad, F.K. and St. Omer, V.E.V. Behavioral and neurochemical
alterations in rats prenatally exposed to 2,4-dichlorophenoxyacetate (2,4-D) and 2,4,5-trichlorophenoxyacetate (2,4,5-D) mixture. Teratology. 37: 515 (1988).


Rohleder, F. Dioxins and cancer mortality - reanalysis of the BASF cohort. Dioxin '89, Abstract # EPI05.


Schulze, G.E. 2,4-D-n-butyl ester (2,4-D ester) induced ataxia in rats: Role for n-butanol formation. Neurotoxicol. Teratol. 10: 81 - 84 (1988a).

Schulze, G.E. and Dougherty, J.A. Neurobehavioral toxicity and tolerance to the herbicide 2,4-dichlorophenoxyacetic acid-n-butyl ester (2,4-D ester). Fund. Appl. Toxicol. 10: 413 - 424 (1988c).


APPENDIX C

Literature Considered by the VA
Advisory Committee By October, 1988
(And Also by the Task Force)


Commonwealth of Massachusetts, Health Survey of Massachusetts Vietnam Veterans. (1986).

Constable and Hatch, "Reproductive Effects of Herbicide Exposure in Vietnam: Recent Studies by the Vietnamese and Others."


Geyer, et al., "Bioconcentration Potential of Organic Environmental


Jensen, "Polychlorobiphenyls (PCB's), Polychlorodibenzo-p-Dioxins (PCDD's) and Polychlorodibenzofurans (PCDF's) in Human Milk,


Lathrop, et al., Air Force Health Study: First Follow-up Examination Results (October 1987).


Ott, et al., "Cohort Mortality Study of Chemical Workers with Potential Exposure to the Higher Chlorinated Dioxins," J.


Stellman, et al., American Legion Vietnam Veterans Study (1985)


USAF School of Aerospace Medicine (AFSC) An epidemiologic investigation of health effects in air force personnel following exposure to herbicides, 6/30/83.


APPENDIX D

Literature Considered by the VA Advisory Committee After October, 1988 (And Also by the Task Force)


Nauman, C.H. and Schaum, J.L. Human exposure estimation for 2,3,7,8-TCDD


Schecter, A. and Ryan, J.J. Polychlorinated dibenzo-para-dioxin and dibenzofuran levels in human adipose tissue from workers 32 years after occupational exposure to 2,3,7,8-TCDD.


Stowell, R.E., et al. Human health aspects of environmental exposure to polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). Universities Associated for Research and Education in Pathology, Inc. Bethesda, Maryland (June, 1988).


Strom, S.C. Issues in biochemical applications to risk assessment: can in vitro studies assist us in species extrapolation?


APPENDIX E

Literature Considered by the VA Advisory Committee at its November, 1989 Meeting
(And Also by the Task Force)


Zack, J. A. and Gaffey, W.R. A mortality study of workers employed