EXTRAPOLATING OCCUPATIONAL EXPOSURE VALUES FROM U.S. EPA IRIS DATA

By

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(Under the Direction of Major Professor Phillip Williams)

ABSTRACT

Occupational exposure values (OEVs) within the United States are developed by various scientific groups which include the United States Department of Labor Occupational Safety and Health Administration (OSHA), the American Conference of Governmental Industrial Hygienists (ACGIH), the National Institute for Occupational Safety and Health (NIOSH), and the American Industrial Hygiene Association (AIHA). These exposure values are believed to provide workers protection to prevent adverse health effects from repeated exposure to a substance day after day. Currently there are approximately 750 chemicals with OEVs, but thousands of chemicals have no established exposure values. The process to establish OEVs is slow and, for many chemicals, limited toxicological data prevent the development of OEVs. Therefore safety and industrial hygiene professionals must make educated assumptions on what is an acceptable chemical exposure concentration. Environmental exposure values, specifically, reference doses (RfD) from the United States Environmental Protection Agency (US EPA) Integrated Risk Information System (IRIS) database do exist for a number of chemicals. In the present analysis, an interim OEV value was derived for 133 chemicals with existing ACGIH Threshold Limit Values (TLVs) using the RfD values from the US EPA's IRIS database. A comparative analysis was then completed between the interim OEV and the existing TLV. This

comparison found that the derived OEV represented a reasonably conservative surrogate value in comparison to the existing TLV, and supports the use of this approach until an OEVs can be established through one of the traditional organizations. Currently the IRIS database contains 200 additional chemicals with no TLV that could be used to develop interim OEVs. Acceptance of this process would provide an interim answer to the limited number of OEVs available for safety professionals and industrial hygienists.

INDEX WORDS: derived OEV, IRIS, reference dose (RfD), Threshold Limit Value (TLV)

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CHAPTER 1

INTRODUCTION

Safety and industrial hygiene professionals are often faced with estimating the potential exposure risk for employees to various substances where no occupational exposure value (OEV) exists. OEVs are used to provide a chemical exposure concentration believed to be acceptable for a worker to encounter day after day without experiencing adverse health effects. There are several sources for OEVs, but currently the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs) provide the most commonly used and up-to-date OEVs. The process to develop additional OEVs or modify existing ones is quite lengthy (1).

The only OEVs with regulating authority are the Occupational Safety and Health Administration's (OSHA) permissible exposure limits (PELs), which were established in 1971 for over 500 chemicals. Except for a few chemicals, these values have never been updated (2). An attempt was made to update the list in 1989, but the courts overturned it in 1993. Recently several studies have reported concern for the limited number of existing OEVs. One study examined high volume chemicals using a simple hazard screening process and found that only 52% of them had OSHA PELs. So, almost half of these chemicals did not have an enforceable OEV. Of the half that did not have an OSHA PEL, 49% had no data available of any kind to even complete a hazard screen (3). The AIHA published a white paper on OSHA PELs stating that " it is a disservice to worker health that the majority of OSHA PELs are based

on recommendations that were made more than 30 years ago." (4). As stated above, the ACGIH has developed the most updated list available and it is a wonderful supplement to assist in setting exposure limits, but there are approximately 688 TLVs in the ACGIH TLV book and there are more than 70,000 chemicals used in industry today (5).

Many companies are taking their own steps to reduce the gap in established occupational exposure limits. Pfizer, a pharmaceutical company, sets internal exposure limits because they believe it is vital for their workers safety. Companies like Pfizer are experimenting with several newly synthesized substances where exposure values need to be developed (5). Currently, the trend in the pharmaceutical sector is establishing performance-based exposure control limits for their pharmaceutical active ingredients because drugs are becoming more potent. These limits are based on the level of control needed for a given operation to maintain risk at an acceptable level. It is not a set exposure limit value but a level of containment that includes engineering controls, safe-handling practices, and administrative procedures combined (6). This is one example of an alternative method to help close the gap that exists with OEVs.

Steps have already been taken to reduce the gap for environmental values, such as reference doses (RfD) and reference concentrations (RfC). The estimated permissible concentration method or EPC method is a process that develops RfD or RfC values from TLVs. This process was initially outlined in the Environmental Protection Agency's *Multimedia Environmental Goals for Environmental Assessment* in 1977. Since its introduction this method or one of similar design has been adopted by several states to derive permissible air emission limits for their air toxics programs (7).

The current study is designed to explore the possibility of another alternative method for developing OEVs, by calculating an interim OEV for chemicals that have available

environmental exposure data. There are a variety of OEVs and environmental values that typically are independent of each other, but some history of overlap exists. For example, the EPC approach discussed above develops environmental values from OEVs and some states use these interim values as their environmental control limits (8,9).

The basis of this study will be the Environmental Protection Agency's Integrated Risk Information System (IRIS)(10). IRIS contains information on human health effects that may result from exposure to chemicals in the environment and the data is based on a 24-hour exposure. This database is updated continuously (10). There are currently 642 chemicals in the IRIS database. All 642 chemicals have descriptive and or quantitative data in the form of oral reference doses (RfD) and inhalation reference concentrations (RfC) for non-carcinogenic health effects, as well as oral and inhalation risks for carcinogenic effects.

Approximately 126 of the IRIS chemicals have established OEVs and the remaining 516 chemicals have no OEVs. So, this database is an ideal source for determining if an interim OEV can be established from environmental data. The project hypothesis is that interim OEVs can be created from existing environmental data, specifically RfC values, and result in a conservative interim guideline for safety and IH risk assessment until a permanent value is set by one of the OEV developing organizations. A test of our hypothesis can be completed using the chemicals in IRIS that have established OEVs, and comparing these values to an extrapolated interim OEV. If a relationship exists between the extrapolated OEV and the actual OEV, it should be possible to develop a method for creating interim OEVs for the remaining chemicals in IRIS in a manner similar to that used in our study.

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CHAPTER 2

LITERATURE REVIEW

Occupational exposure values (OEV) are a necessity to provide a safe and healthy working environment for workers over their employment lifetime. Without these values individuals could be exposed to hazardous environments without any guide to protect them. We have progressed significantly over the years in providing effective procedures for protecting workers, but gaps still exist. We use and make thousands of chemicals on a daily basis and only a small percentage of these chemicals have OEVs.

Researchers initially proposed OEVs in the 1880s. In 1930, the USSR was the first country to actually publish an official list through its Ministry of Labor (2). By the 1930s, in the United States and in Europe, several lists of exposure limits were published (1). In 1937, the Division of Industrial Hygiene was created in the United States as part of the National Institute of Health (3). This group's mission was to conduct extensive analyses and evaluate various methods related to collection of chemical samples in the workplace (4). In 1946, this group became apart of the Division of Occupational Health. The following sections will provide a general overview of the principal OEVs and environmental exposure values used in the U.S.

Threshold Limit Values

In 1938, the National Conference of Governmental Industrial Hygienists (NCGIH) was established as an independent body initially comprised of two representatives from each

governmental industrial hygiene agency. It's first meeting consisted of 76 members that included 24 states, 3 cities, a university, the U.S. Bureau of Mines, the Tennessee Valley Authority, and the U.S. Public Health Service (5). This meeting generated nine standing committees that were charged to address industrial hygiene issues related to the pre-war era. The committees included: "appraisal methods, relationships with industry, labor, the medical profession and other agencies, technical standards, education, uniform reporting of occupation diseases and other illnesses among workers, administrative development of state activities, industrial health code, legislation, and personnel" (5). These were the first steps towards establishing occupational exposure limits in the United States.

In 1946, the NCGIH changed its named to the American Conference of Governmental Industrial Hygienists (ACGIH) and also offered open membership to all industrial hygiene personnel that worked within state or federal agencies and also governmental industrial hygienists in other countries. In 1941, the ACGIH established the Threshold Limit Values (TLV) for Chemical Substances Committee. It was a standing committee by 1944 and its duties were the investigation, recommendation, and annual review of exposure limits for chemical substances. In 1946, this committee published and adopted is first list of exposure limits for 150 chemicals that at the time were termed "Maximum Allowable Concentrations"(6).

During the 1940's increased concerns arose about worker exposure to chemicals partially due to the development of the atomic bomb program. Herbert Stokinger was one of the key pioneers in developing sampling methods and carrying out inhalation studies for developing exposure limits. His first work was with the atomic bomb program where he completed inhalation studies on uranium, beryllium, and other toxic materials that could be released from the atom bomb project and expose workers (3).

Stokinger was a key member of the Division of Occupational Health in the 1950's. He was in charge of the Toxicology Division. He helped improve the experimental designs of toxicology studies to help obtain more accurate data to establish accurate occupational exposure limits. He was also a key member of the TLV Committee of the ACGIH for more than 15 years. During his membership the committee introduced the term "Threshold Limit Values" in 1956 and in 1962 published the first "Documentation of the Threshold Limit Values"(3).

Stokinger also helped set the key principles for establishing TLVs. The basic philosophy or beliefs of the committee were:

- TLVs are health-based recommendations derived from the review of published scientific information from human and animal studies. Each TLV will have published documentation supporting the recommendation from the committee.
- TLVs are based on thresholds of response, meaning no adverse health effects would occur in workers – including those set for carcinogens.
- TLVs refer to airborne concentrations that nearly all workers may be exposed to for 8 hours a day, 40 hours per week without adverse effects for a working lifetime. Due to variation in susceptibility, the recommended TLVs may not protect some workers.
- TLVs are not fine lines between safe and unsafe conditions. They are guidelines for the practice of industrial hygiene and should not be used by anyone untrained.
- TLVs are derived from an open process. A provisional list is made of recommended additions or amendments to existing TLVs through Notice of Intended Changes (NICs), for a minimum of two years to allow for input from interested parties. The TLV committee will meet with interested groups to hear point of views. Lastly,

recommendations are made and published with the scientific basis for the judgement (6).

Permissible Exposure Limits

In 1970, the Occupational Safety and Health Act, established the Occupational Safety and Health Administration or OSHA (7). OSHA's creation was designed to provide safe and healthy work environments for workers. This has basically been completed through the development of mandated safety and health standards (7).

OSHA developed the Permissible Exposure Limits (PELs) standard based primarily on the 1968 ACGIH TLV values and the American National Standard Institutes recommendations. The PELs were promulgated in 1971 and contains exposure values for more than 500 chemicals. The majority of these values have not changed, even though new toxicological and other available data on various chemicals have. The only significant changes that occurred were the addition of 24 substance-specific standards and three general standards or rules (Cancer Policy, Access to Employee Exposure and Medical Records, and the Hazard Communication standard) (7).

Workplace Environmental Exposure Limits

In 1976 the AIHA developed a committee called the WEEL committee. This group was responsible for setting workplace environmental exposure limits (WEELs). This committee's principal goals were as follows:

- Gathering and evaluating information related to setting exposure limits.
- Developing exposure limits for substances when no other legal authoritative limit exist.

- Providing an open forum for development of exposure guidelines for chemical, biological, or physical indices (8).

The WEEL committee consists of approximately 30 members from government, industry, labor, and consultants and the group meets three times a year. This group also communicates with the ACGIH TLV committee. The WEEL values are expressed in the form of 8-hour time weighted averages, short-term exposure limit or a ceiling value. Notations are also added if a substance is deemed a skin irritant, dermal sensitizer, or respiratory sensitizer. These values are derived from human and animal data with a safety margin included (8).

Recommended Exposure Limits

NIOSH, which is the National Institute for Occupational Safety and Health, also has established exposure limits termed Recommended Exposure Limits or RELs. They began developing these values in the 1974 when they joined OSHA in developing the Standards Completion Program. This program established occupational health standards for chemicals with existing PELs (9). From this program the NIOSH RELs were created. NIOSH RELs are based on criteria documents, current intelligence bulletins, alerts, hazard reviews, and legal testimony. A complimentary feature of the REL is a criteria document that contains guidance for addressing worker training, exposure monitoring strategy, sampling and analytical methods, engineering controls, personal protective equipment, medical surveillance and screening requirements as well as record keeping (8).

RELs are developed through selection prioritization, review of scientific literature, internal and external reviews and dissemination through publications and the NIOSH web site (10). NIOSH RELs are primarily set from qualitative assessments and follow these 4 principles:

- A systematic approach to identify significant occupational health and safety hazards whose risk factors may cause occupational disease or injury.
- An evaluation of the hazard is made in terms of how the exposure can occur, the extent of exposure, and the number of workers exposed.
- A scientific review of the health data, including identifying biases related to a study's analysis.
- Levels of exposure are set for no observed adverse health effect (10).

Following these principles, NIOSH has established RELs for over 677 chemicals (9).

American National Standards Institute

ANSI, the American National Standards Institute, has a Z-37 Committee that sets workplace quality standards called maximal acceptable concentrations. These values are 8-hour time-weighted averages like the TLVs.

The Z-37 committee is a group of governmental, industrial, professional, and university experts that work in the areas of industrial hygiene, toxicology, and/or medicine. The members of the committee are given assignments for standard development and the whole committee votes on whether the standard should be sent forward for Institute approval and finally publication (11). The Maximal Acceptable Concentrations are available for several substances in individual documents, which outlines the basis for the limits. Analytical and sampling methods are described as part of the publication as well as the toxicity of the material and its chemical and physical properties.

New Chemical Exposure Limit

The EPA developed an exposure limit program in the 1980s called the New Chemical Exposure Limit program (NCEL) (8). Its design was to help establish interim occupational

exposure limits for new chemicals used in the United States. The general guidelines followed in developing these interim exposure limits were as follows:

- To promote engineering controls and reduce reliance on respirators as a control.
- To resemble the OSHA PEL or basic format and ideology.
- To not overlap OSHA PELs, but to co-exist. (Meaning NCEL values are void if an OSHA PEL is developed for the same chemical).

EPA's NCEL program suffers from the same issues all groups do that are setting exposure limits: lack of appropriate data in the form of exposure or toxicological data. Typically NCEL values are based on analog data and historical data from other chemically similar substances and exposures (8). The analog data is toxicological data for a substance that has a similar chemical structure to the chemical with the exposure limit. The end points of this data are usually no observed adverse effect level (NOAEL) or lowest observed effect level (LOAEL). Then an uncertainty factor is added to account for variability in sensitivity to the material and variability of individuals before a NCEL is created.

Using analogy as a means to calculate a new chemical's exposure limit has two key limitations:

- Inconsistency of the qualitative effect: A chemical in the same family may respond completely different when compared to others within the same family.
- Inconsistency of the quantitative effect: Similar to the statement related to qualitative effects, but using this may be even more hazardous.

To illustrate the limitations more clearly, let's say we have a chemical family that's shown to cause reproductive problems in animal studies for 75% of that family. If we have a new member

to this family with no toxicological data available and we assume through analogy that this material is a reproductive hazard as well, we may be setting limits incorrectly (11).

How Are Occupational Exposure Values Established

Each organization has distinct methods of selection, prioritization, and required scientific documentation for selecting a chemical for OEV development. NIOSH RELs and AIHA WEELS processes were briefly discussed in the prior section. The focus of this section is on OSHA and ACGIH OEV methods because OSHA PELs are the only exposure values that are mandatory, enforceable values. ACGIH TLV values are the most commonly used and recognized worldwide because they are the largest up-to-date list of exposure values available today. ACGIH has about 688[(19)] exposure limits, where there are only 60 WEELS and NIOSH has developed 677[(9)] REL values but most of these are already covered by ACGIH and OSHA (12).

Under the OSHA Act, agents or chemicals are selected for consideration for standard-setting on the basis of information submitted to OSHA "by an interested person, a representative of any organization of employers or employees, a nationally recognized standard-producing organization, the Secretary of Health and Human Services, the National Institute for Occupational Safety and Health, or a State or political subdivision, or on the basis of information developed by the Secretary [of Labor] or otherwise available to him." (29 USC sub sec. 655 1990). Although a chemical may be recommended to OSHA for selection, in order for an Act or Standard to be accepted, OSHA must prove that there is a significant risk of health impairment if the standard is not established. If approved, prioritization of developing the standard is based on two factors: Urgency of the need for the standard, and recommendations of the Secretary, Division of Health and Human Services (7).

The OSHA standards are based on extensive reviews of all available information, which includes, but is not limited to the following:

- Scientific literature, including human and animal studies.
- Existing exposure limits in other countries.
- Information from other agencies and institutions.
- OSHA's own quantitative risk assessments.

The quantitative risk assessment OSHA completes must meet the requirements for justifying the necessity of developing a specific safety and health standard.

OSHA has two categories of standards that are developed for chemicals relative to exposure values. They are PELs, which is simply establishing a safe exposure value or PEL, and then a more comprehensive standard that includes both the PEL, and the requirements for exposure monitoring, medical surveillance, training, hygiene facilities, protective clothing and equipment, and any other necessary information (13). There are about 500 OSHA PELs established and 26 specific chemical standards (13, 14).

The final step in OSHA's process is the feasibility study followed by the review and approval process. If the proposed standard is shown to be a feasible option then steps are taken to have the standard approved as a rule. This process is quite extensive including several review periods and can typically take several years to complete (7).

One of the key problems with existing PELs, which are our only regulated occupational limits, is that the majority is based on research conducted primarily in the 1950s and 1960s. Thus PELs are outdated (15). OSHA did update limits and added 164 more substances to their list based on information from ACGIH in 1989. The courts overturned that action in March of 1993 because OSHA did not follow their own guidelines for updating and adding new values

which included completing their own risk assessment for each change. Instead, they relied only on the information from ACGIH (16, 17). Although the values did not become mandated, OSHA did suggest that if an industry did not follow the new values proposed by ACGIH, they could be fined under the general duty clause in certain circumstances (18).

The American Conference of Governmental Industrial Hygienist (ACGIH) is a non-profit, non-governmental corporation. Its organization is a mix of health and safety professionals. As stated before, the ACGIH does not set standards. It is a scientific group that has committees that review currently published scientific literature. The ACGIH proposes guideline values known as TLVs and Biological Exposure Indices (BEI) to help safety and industrial hygiene professionals make sound decisions relative to exposure levels to chemicals and physical agents in the workplace. Several local, state, and national governments consider the work of the ACGIH to be standards that can be actionable by law.

When a chemical is selected by the ACGIH for the development of a TLV or for review of an adopted value, the chemical is placed in the "Under Study" list. This list is published annually for interested groups to provide assistance to the committee on the development by sending any available relative data. One major difference between the OSHA and ACGIH processes is that the feasibility studies required by OSHA are not considered in the ACGIH process when developing or adopting a new TLV.

Members of the ACGIH committee are then selected to collect all the information and data available to develop draft TLV *Documentation,* which is a general review of the literature relevant to developing a new TLV. This *Documentation* is then reviewed by other specific committee members and then by the full committee until a final draft is completed. Once the draft is accepted, it is sent to the ACGIH Board of Directors for ratification. If the proposed

TLV is accepted it is published in the Notice of Intended Changes section of the Annual Report, and other ACGIH publications. This proposed TLV is considered a trail limit typically for one year. During this time, interested parties can bring forth information and comments. If no evidence indicates that the proposed TLV is unacceptable, then the Committee and Board of Directors consider it for adoption. Once ratified, the new TLV is published in the Annual TLV and BEI book (19).

How are Environmental Exposure Values set?

The United States Environmental Protection Agency (EPA) has exposure values established for over 642 chemicals relative to protecting the general public. These exposure values can be found in the U.S. EPA IRIS database, which is an electronic database containing the values that have been set and the supporting toxicology data that was used to help establish these values. The environmental exposure values for non-carcinogenic effects are in the form of oral and inhalation exposures only. The general terms used for non-carcinogenic effects are reference doses (RfDs) for oral exposures and reference concentrations (RfCs) for inhalation exposure (20).

The EPA uses risk assessment and risk management tools in setting their protection factors for the general population. They use the risk assessment tool to determine the potential exposure severity of a group of people to a particular chemical, thereby developing an estimate to be made of the present or potential health risk to the group. The information for the risk assessment is then used in the risk management process to decide how to protect the general public's health. An example of a risk management action is setting acceptable levels for air emissions (11, 21). So, in summary, the risk assessment provides the information about the health risk that later provides the action from the risk management review.

IRIS is EPA's main tool for providing accurate and up-to-date risk assessment information. It helps provide hazard identification and dose-response assessment information, but no situational information on individual instances of exposure. The IRIS data does differentiate its information for carcinogenic and non-carcinogenic chemicals. When it is combined with specific exposure data, IRIS can be used for characterization of the health risks for a given chemical in a given situation that can lead to designation of a risk management decision (22).

The following steps are taken to add assessments to the IRIS database. Step one is an annual announcement in the Federal Register of EPA's IRIS agenda and a call for available scientific information about the selected chemical substances from the public. Second a search of the current literature is completed. Then draft health assessments and IRIS summaries are developed. A peer review is completed within the EPA and then outside the Agency. If there is a consensus in EPA and management approval, final IRIS summaries and supporting documents are prepared and then entered into the IRIS database (23).

Types of Occupational and Environmental Exposure Values

Based on temporal exposure, there are three categories of occupational exposure values. They are the Time Weighted Average (TWA), Short-term exposure limit- STEL, and the Ceiling Limit- CL.

- The TLV is the time weighted average concentration for an 8-hour day and a 40 hour workweek, to which repeated exposure day after day at this level or below will cause no adverse effect.
- The STEL is a 15-minute exposure that should not be exceeded at any time during the workday, even if the 8-hour TLV is within acceptable limits. STEL exposures should

not be longer than 15 minutes and should not occur more than 4 times a day. There should be an hour or greater break between these exposures in this range.

- The ceiling limit is the concentration that should never be exceeded during any working exposure (19).

There are three categories of environmental exposure values. They are: the reference dose (RfD), the reference concentration (RfC), and the carcinogenicity assessments. The RfD and RfC are estimates of a daily exposure to the general public that should not cause adverse effects during a lifetime. These values include all populations including sensitive groups like children. The RfD and RfC values are derived from non-carcinogenic effects of a chemical. The RfD is the oral exposure concentration and the RfC is the inhalation exposure concentration (24).

The carcinogenicity assessment first looks at the likelihood of a chemical to be carcinogenic for humans. Then a quantitative assessment is completed, which includes the development of an oral slope factor and oral and/or inhalation unit risks. The oral slope factor is the calculated human cancer risk by body weight and by day. The unit risk is estimated from the oral slope factor in terms of the risk from drinking water or the risk from breathing an air contaminant concentration (25).

Limitations of IRIS Data

The IRIS database is key in supporting the hazard identification and dose-response steps of the EPA's risk assessment process because of all the valuable information contained within the database. This project is evaluating the possibility of extrapolating occupational exposure values from the current RfD or RfC, which are environmental values established from daily exposures over a lifetime, including sensitive populations.

There could be added uncertainty when trying to extrapolate the data from a daily lifetime exposure to a more direct 8-hour exposure. Other uncertainties are the extrapolations from animal data to humans and from high experimental doses to lower environmental exposures. In particular, the adverse effect observed in an animal study from a chemical exposure may be completely different than the end result in humans (25).

Other considerations about environmental data are in the acceptability of the toxicological studies. Typically no adverse effect levels (NOAEL), lowest observed adverse effect level (LOAEL), or no observed effect levels (NOEL) are the end point of these studies. Frequent questions around these endpoints are related to a number of factors: sensitivity of the animal species used in comparison to man, the number of animals (one species) used in the study, and the dose ranges of the chemical used in the study (11).

Limitations of TLVs

Although ACGIH TLVs are widely accepted across the world, these values have been debated. When West Germany and Holland adopted the use of these values, they re-evaluated the science behind the TLVs and found that there was only adequate scientific information for only 10% of the TLVs. The main deficiency was insufficient data on long-term exposed workers, followed by insufficient data on long-term exposure to animals, and last the development of exposure limits for a chemical based on analogy to other chemicals versus specific-chemical data. These deficiencies are related to the toxicological information that helps establish the exposure limits. This does not mean the current TLVs are incorrect, it just illustrates the problems that exist in developing exposure limits (26).

Other concerns or limitations related to TLVs are that, in general, limits do not take into account multiple routes of exposure (27). Also, the process in general for getting a chemical on

the ACGIH list can take years. Under its structure it can take as little as two years for a new limit to be adopted, but it may take years before a substance is seen by the committee and is set as a priority (12).

Stokinger, the pioneer in establishing TLVs was concerned with the TLV protection to special risk groups. Five to ten percent of workers can possess an undue susceptibility to certain substances found in the work environment because of genetic and biological factors. He believed these individuals should be identified because they are at special risk since standards like TLVs are designed for the average person and do not protect those who are more susceptible (28). Of course this view has been controversial, but illustrates the fact that TLV do have limitations.

Generating New OEVs

Currently there are two studies published that have positively shown that there is a strong link between occupational exposure limits and environmental limits. These two studies both showed that environmental limits could be established from existing occupational exposure limits.

The first study looked at developing interim estimated permissible concentrations (EPCs) for 103 chemicals that did not have an existing reference dose or concentration. It was reported that the EPC calculated values represented a conservative interim environmental exposure value (29). The methodology used in the study went as follows:

- EPCs were calculated by adjusting a 40 hours/week to a comparable 24 hours/7days per week. (Dividing the TLV by 4.2)
- Safety factor of 10 was then added to account for sensitive populations and an additional 10 from Multimedia Environmental Goals suggestion (Cleland and Kingsbury, 1977)
- The mg/m^3 number and RfC values could be directly compared to the EPC air value.

- To compare to Oral RfD values the EPC_{air} value must be converted further to mg/kg/day.

Comparisons for the study were completed using a simple ratio analysis. This analysis was completed on all 104 chemicals that had a TLV and a RfD or RfC. An additional analysis was completed to see if changes over-time might effect the ratio results. They compared 1990 data in this part. Lastly, a "EPC-associated uncertainty factor" ratio was calculated for chemicals that had an initial ratio of greater than 5. This is the value resulting from dividing the uncertainty factor used in the USEPA chronic RFD by the EPC to RfD ratio. When ratios were compared, 82% were less than 1.0 (84 of 103) when comparing subchronic RfD or RfC to EPC values. When ratios were compared 57% were less than 1.0 (59 or 103) when comparing chronic RfDs or RfCs to EPC values. To summarize, EPC values are more conservative 3 out of 4 cases for subchronic RfDs or RfCs and 3 out of 5 cases for chronic RfDs or RfDs. So, this study found that the EPC values would provide a great interim until sufficient toxicology data is available to develop a set value (29).

The second study evaluated the EPC approach to develop health-based soil and water screening concentrations for environmental chemicals (30). This study reviewed 30 chemicals that had TLVs and where on EPA's Appendix VIII Hazardous Constituents list, but did not have an established RfD or RfC. The researchers believed that the interim values that could be created would be beneficial in developing acceptable toxicity concentrations in soil and water for humans. They calculated interim RfD and RfC values using the same formula as the first study and then added that value into the basics equations for intake of soil and intake of water. The end result is they found that the interim values filled a void that existed in the risk assessment processes, where no federal, state, or environmental guidelines have been established (29).

Environmental and occupational exposure values are very similar in design. Both generally are based on either animal data or human data. The only key difference between them is the amount of time for an exposure and the exposed population. Uncertainty factors are margins of safety set to account for the limitations in the toxicological data, and they are a key part of developing the RfD or RfC. For example, NOEL or NOAEL is the end point used for most toxicological studies for non-carcinogens because limits are based on the "no effect" level which is defined as a level which will not produce deleterious effects on human health or overload the normal mechanisms that protect the individual (30,31). When the endpoint is not a NOEL or NOAEL, but a LOAEL an additional uncertainty factor may be applied to establish a value that will result in no effect.

TLVs like RfD or RfC values also have a margin of safety because of the inadequacies with toxicological data. Typically the margin of safety is between the lowest effective dose and the proposed TLV. If you were to express this mathematically this would be TLV = lowest effective dose/ safety factor. The range of the safety factors for ACGIH values are estimated to be between 0.2 and 10 (32).

Conclusion

Due to the similarities associated with the development of TLVs and RfD values and the past studies using the EPC approach to extrapolate RfD and RfC values from existing TLVs, the study presented in Chapter 3 was conducted. RfD values were compared to the same chemicals' TLV and the relationship between the two exposure values was compared. The study presents the results of the analysis and makes recommendations for implementation of a proposed interim OEV process as an alternative means to help reduce the gap that exists for setting occupational exposure limits.

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CHAPTER 3

EXTRAPOLATING INTERIM OCCUPATIONAL EXPOSURE VALUES FROM U.S. EPA IRIS DATA[1]

[1]Woodgeard, Heather; Manning, Randall; and Williams, Phillip L. To be submitted to *Regulatory Toxicology and Pharmacology.*

ABSTRACT

Occupational exposure values (OEVs) within the United States are developed by various scientific groups which include the United States Department of Labor, Occupational Safety and Health Administration (OSHA), the American Conference of Governmental Industrial Hygienists (ACGIH), the National Institute for Occupational Safety and Health (NIOSH), and the American Industrial Hygiene Association (AIHA). These exposure values are intended to provide workers protection to prevent adverse health effects from repeated exposure to a substance. Currently there are approximately 750 chemicals with OEVs, but thousands of chemicals have no established exposure values. The process of establishing OEVs is slow and, for many chemicals, insufficient toxicological data limits the development of OEVs. Therefore safety and industrial hygiene professionals must make educated assumptions on what is an acceptable chemical exposure concentration. Environmental exposure values, specifically, reference doses (RfD) from the United States Environmental Protection Agency (USEPA) Integrated Risk Information System (IRIS) database do exist for a number of chemicals. In the present analysis, an interim OEV value was derived for 126 chemicals with existing ACGIH Threshold Limit Values (TLVs) using the RfD values from the US EPA's IRIS database. Then the interim values were compared to the existing TLV. This comparison found that the derived OEV represented a reasonably conservative surrogate value when compared to the existing TLV, and supports the use of this approach. Currently the IRIS database contains 200 additional chemicals with no TLV that could be used to develop interim OEVs. This process would provide an interim answer to the limited number of OEVs available for safety professionals and industrial hygienists.

Keywords: derived OEV, IRIS, reference dose (RfD), Threshold Limit Value (TLV)

INTRODUCTION

Occupational exposure values (OEVs) are used by safety and industrial hygiene (IH) professionals as a means to assess the risk of exposure to various substances in the workplace. OEVs are available for approximately 750 chemicals and there are four key organizations that currently develop OEVs in the United States. They include the American Conference of Governmental Industrial Hygienists (ACGIH) who develop Threshold Limit Values (TLV), OSHA who establishes Permissible Exposure Limits (PEL), the National Institute for Occupational Safety and Health (NIOSH) who develop Recommended Exposure Limits (REL), and the American Industrial Hygiene Association who develop Workplace Environmental Exposure Limits (WEEL) (See Table 1). For many chemicals, however, OEVs do not exist, and the safety and IH professionals must rely on professional judgement.

Given that only around 750 chemicals have established OEVs, there are countless exposure situations in the workplace where no OEV exists. Furthermore, given the length of time required to develop a new value through the traditional approach, the need exists for the development of interim OEVs that can provide employees some protection.

The US EPA uses environmental exposure values to assess risks to the entire population. These values are expressed as either reference doses (RfD) or reference concentrations (RfC) that can be found in EPA's Intergrated Risk Information System (IRIS). The RfD and RfC values are derived from animal studies data like many OEVs, but are established based on protecting the entire population throughout their lifetime, where OEVs, are based on a subset of the population, workers, during their employment years. More specifically, OEVs do not

account for sensitive populations, children and the elderly, and only cover a portion of an individual's day (usually 8 hours of a day or 40 hours per week).

An approach that uses environmental exposure values to drive OEVs may fill the gaps for substances that do not have OEVs. Earlier studies completed by the US EPA for the development of interim environmental exposure values termed EPCs (estimated permissible concentrations) completed the reverse calculation using OEVs to generate environmental exposure values (Cleland and Kingsbury, 1977). In 1994, analysis demonstrated that the calculated EPC values were safe environmental exposure values for over 100 chemicals that had both TLVs and environmental exposure factors (RfDs and RfCs). Several states adopted the interim EPC-values or the EPC approach to set permissible air limits for their environmental programs (Williams et al, 1994).

This project proposes that interim OEVs can be developed using an approach similar to the EPC method, but in the reverse. Basically interim OEVs can be established based on existing environmental values, specifically the study data used to set RfDs. The analysis will focus on TLV exposure values from the 2003-2004 ACGIH guidebook (ACGIH, 2003) and RfD study values from US EPA's IRIS database (EPA, 2003). RfD values were chosen over RfC values, because currently there are more RfD values available. Both of these values are recognized as acceptable indicators for occupational and environmental exposures, respectively. In particular the ACGIH TLV list is the most current and comprehensive values available for occupational exposures to chemicals, and they actually served as the primary basis of the original OSHA PELs (permissible exposure limits) standard (54 Federal Register, January 19,1989). The IRIS database is continuously updated and is the most comprehensive listing of environmental exposure values (USEPA, 2003). Establishing interim OEVs would greatly improve the

predictability of setting accurate protection guidelines for workers who work with chemicals that have no OEV. These values would provide safety and industrial hygienist (IH) professionals more quantitative data to assess the risk, then strictly relying on professional judgement.

MATERIALS AND METHODS

The project analysis used all chemicals in IRIS that had both TLV and RfD values, a total of 126 chemicals. The first step of the analysis converted the oral RfD value in units of mg/kg/day to an air value in units of mg/m^3, which is used for TLVs. This step was accomplished by using equation 1 in Figure 1 (Williams, 1981). For each oral RfD study value used, the IRIS database was reviewed and the variables identified. In some cases, No Observed Adverse Effect Level (NOAEL) values were not available and, in those cases, the most stringent available value was used. These values would include lowest observed adverse effect level (LOAEL) and lowest effect level (LEL).

An application of equation 1 is illustrated using Acetone as an example (See Figure 2). For Acetone, IRIS used the NOAEL value of 100 mg/kg/day with a UF of 1000. Using these values, the oral RfD is converted to an equivalent air concentration. The conversion shown with equation 1 was completed for 126 chemicals from IRIS that had oral RfD study values and existing 2003-2004 TLVs. For all TLVs, air concentration of mg/m^3 were used by converting ppm values using equation 2 in Figure 3 (ACGIH, 2003).

The next step in the analysis compared the existing TLVs with the OEVs calculated from RfDs. This step was followed by a simple comparison of the two values by calculating the ratio between them as shown in equation 3 in Figure 4.

Using equation 3, ratio analyses were completed for all 126 IRIS chemicals.. The ratio values were then plotted to determine the number of chemicals that had a ratio less than one, which indicates a more conservative value then the existing TLV.

Next, the chemicals were divided into groups based on the type of toxicological study on which the RfD values were based: chronic animal studies, subchronic animal studies, and human studies (includes both chronic and subchronic). These values were compared using the same ratio criteria provided above.

Finally, a third comparison was made by applying different uncertainty factors (UF) to the ratio criteria from equation 3. The calculations discussed to this point used the UF provided from the IRIS toxicological study used for each chemical. These values were identified based on protection of the general population. Since OEVs protect only working populations, a lower UF may be more appropriate. Two additional UF values were used for comparison with the existing IRIS UF. They are a "modified" UF that eliminated protection for sensitive human groups from the study, and an "adjusted" UF that uses simple basic toxicological principles for setting a UF . The basic principles are listed for determining the UF. Typically a 10-fold default factor is used in deriving the RfD from the experimental data, but it can be smaller.

-Uncertainty in susceptibility among the members of the human population or intraspecies differences.

- Uncertainty in extrapolating animal data to humans or interspecies differences.

- Uncertainty in extrapolating from data obtained in a study with less-than lifetime exposure (subchronic to chronic exposure).

- Uncertainty in extrapolating from a LOAEL rather than from a NOAEL.

- Uncertainty associated with extrapolation when the database is incomplete (14).

Lastly the ratio values were divided into smaller subgroups in a similar manner as the EPC study (Williams et al, 1994).

RESULTS

Table 2 provides a summary of the 126 chemicals from IRIS that were used in the study. The table includes the chemical name, TLV (in mg/m^3), toxicological study that was the basis for the RfD, and calculated OEVs and ratios. Four of the 126 chemicals had multiple studies with NOAEL values associated with them: atrazine (2), barium (3), cadmium (2), and endusulfon (2). For these chemicals, each study was used for the conversion resulting in a total of 131 conversions for 126 chemicals.

To determine if the OEVs calculated from RfD studies are reasonably conservative, the values were compared to current TLVs for all 126 chemicals (includes extra results for four chemicals with multiple studies) using the ratio results. Table 3 summarizes the results of the comparison. As shown, regardless of the UF conversion approach, the OEV values were more conservative than the current TLVs for 83% of the chemicals. The table also shows that the chemicals were also grouped into 3 subgroups according to the type of study used to calculate the RfD: subchronic animal studies, chronic animal studies, and human studies. The subchronic animal studies resulted in a more conservative value for 78% of the chemicals, the chronic animal studies results were more conservative for 81% of the chemicals and the human studies results were more conservative for 92% of the chemicals (independent of the UF conversion value).

The ratio results listed in Table 3 were distributed into ranges (Figure 6). As shown in Figure 6, regardless of the UF conversion used (390 values, which is all UF calculations), 21%

of the data had a ratio greater than 1, and 79% of the data had a ratio of less than 1. If the data compared each UF conversion separately, the percentages change. For the data calculated using the UF from the IRIS study: 11% had a ratio of greater than 1 and 89% had ratios less than 1. The percentages for the adjusted UF ratios were 15% greater than 1 and 85% less than one, and the modified UF ratios were 27% greater than 1 and 66% less than 1. Figure 6 is based on the percentages above and illustrate that the UF from the IRIS study and the adjusted UF have more ratios less than one and the modified UF has slightly more ratios that are not as conservative and were greater than one.

DISCUSSION

The objective of this study was to determine if useful OEVs could be extrapolated from EPA's IRIS database, specifically from oral RfD values. It is estimated that over 70,000 chemicals are used in industry and that only approximately 750 have established OEVs (see table 1). Consequently, this study could provide an interim solution for protecting workers until permanent exposure values are set by one of the various organizations.

The OEVs were calculated from RfDs and compared to the current TLVs for the 126 chemicals in EPA's IRIS database (See Table 3). The results (average percent of all three UF results for that particular study) show that the derived OEVs are more conservative than the current TLVs for 78% with subchronic studies, 81% for chronic studies, and 90% for human studies (Table 3). If the data is divided and reviewed based on the selected UF that was used, 89% of the OEVs developed from the IRIS UF or adjusted UF are more conservative. Even using a smaller UF, the modified UF, resulted in 73% of chemicals with OEVs less than the

current TLVs. For all results together, independent of the study type, the OEVs calculated from oral RfD values were more conservative 83% of the time. In general, the most conservative OEVs result from chemicals with RfD values based on human studies. The modified UF, which eliminated the protection for sensitive groups, provides the least conservative approach. Therefore, the OEVs calculated from RfDs are generally conservative enough for potential use as an acceptable surrogate exposure value for those chemicals that currently do not have established OEVs until such time a value could be established by an organization such as the ACGIH.

The analysis was taken a step further and the ratio values were broken down and distributed (Table 3). For the data calculated using the IRIS UF from the RfD study and Adjusted UF approximately 89% and 85% respectively have ratios of less than 1. For the Modified UF data there were ratios of less than 1 for approximately 66%. The significant difference between the modified UF values percentage and the other two UF values resulted because the modified UF typically removed a factor of 10 for approximately 90% of the data to remove protection for sensitive populations. This was completed to see if the values obtained would be similar to existing TLV values which are designed to protect a subgroup that does not contain protection for sensitive individuals like children (Nighswonger, 2000). These results show that the elimination of that factor is not necessary. Using the UF from the RfD study or one based on the simple toxicological basics is better.

As stated in the results, data from all UF groups were plotted (Figure 6). The ratios calculated using the adjusted and the IRIS RfD study UF illustrated that the interim OEVs calculated were more conservative than the current TLV for a large number of chemicals. The ratios calculated using the modified UF indicated that the interim OEVs calculated were not as conservative than the current TLV with slightly more ratios above 1. These results also show that

even if the UF factor is adjusted to remove protection for more sensitive populations, the resulting OEV provides a good interim exposure value for protecting workers until one of the traditional groups can established an OEV.

Although this approach is simplistic in design, it is very straightforward and easy to use. Furthermore, the approach is similar to one presently used by the ACGIH to establish TLVs. To be more specific, 24% of the TLVs established by ACGIH are based on the process of analogy. Analogy is establishing an exposure limit for a chemical based on using the TLV of another chemical with similar structure or properties. (ACGIH, 2003). Currently the EPA generates New Chemical Exposure Level (NCEL) values (EPA, 1985). These values are developed and designed to be interim OEVs based on their available toxicology data until a permanent PEL is set for the chemicals (Lentz, 2001). The majority of NCELs are established by comparison of chemical analogies.

Several recent studies have shown that environmental values, RfDs and RfCs, can be extrapolated from occupational exposure values. These studies include the two EPC approach reports that Williams et al (1994) completed. His first study developed acceptable interim RfD and RfC values from TLVs and in the other study developed acceptable interim soil and water concentrations from TLVs (Williams, 1994, 1995). Prior to Williams et al (1994, 1995) group's work, in 1986 Calabrese was able to demonstrate that ambient air quality standards could be developed that were more conservative than the present standards from TLVs (Calabrese, 1986).

In conclusion, OEVs are needed for protecting workers using thousands of chemicals with no established OEV set by any regulatory or scientific body. The calculations for developing the OEV from environmental values are quite simple, and could supply safety and IH professionals with an interim exposure value for chemicals that do not currently have established

TLV. This process will help close the gap that exists in the area of occupational exposure limit development. It is not intended to replace the processes that currently exist through our various regulating and scientific bodies, like OSHA or ACGIH, but to supplement them until permanent values can be established. Given the conservative nature of the exposure values that are likely to be produced and the need for guidance values to protect workers from the risk of exposure we believe the interim OEV process would be a useful mechanism in reducing risk and assessing exposure potentials. If this method was applied today an additional 238 OEVs (listed in table 4) could be available for use and new ones could be added when EPA generates new RfD studies, which based on the last two years chemicals added would be around 4 or 5 new OEVs yearly, which is a 35% increase in the average number that are created every year by the ACGIH TLV committee.

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Table 1 – Current Available Occupational Exposure Limits[1]	
Organizations – Exposure Value	Number of chemicals with these values
ACGIH – TLV [13]	688
OSHA – PEL [8]	500
NIOSH – REL[16]	677
AIHA – WEELS[17]	60

1 - Although 1915 occupational exposure values are available, there is overlap across several of the organizations resulting in approximately 750 individual chemicals with OEVs (i.e., all OSHA PELs were derived from TLV and REL values).

Table 2: Summary of Data Analysis										
NO	**Chemical Name**	**TLV (mg/m^3)**	**Chosen Study Factor**	**Interim OEV Air Conc. from IRIS**	**OEV from ADJ**	**OEV from MOD**	**Ratio IRIS OEV/TLV**	**Ratio ADJ OEV/ TLV**	**Ratio Mod OEV/TLV**	**Study**
1	**1,3-Dichloropropene (542-75-6)**	4.5	5.1	0.446	0.446	4.463	0.099	0.0992	0.9917	Rat Chronic feeding study
2	**112-Trichloro-122-trifluoroethane (76-13-1)**	7665	273	238.875	238.87	2388.75	0.031	0.0312	0.3116	Epidemiological study: Human occupational exposure
3	**112-Trichloroethane (79-00-5)**	54.6	3.9	0.034	0.034	0.341	0.001	0.0006	0.0063	Mouse subchronic drinking water study
4	**123-Trichloropropane (96-18-4)**	60.3	5.71	0.050	0.050	0.500	0.001	0.0008	0.0083	Rat oral subchronic study
5	**124-Trichlorobenzene (120-82-1)**	37.1	14.8	0.130	0.130	1.295	0.003	0.0035	0.0349	Rat reproductive study
6	**246-Trinitrotoluene (118-96-7)**	0.1	0.5	0.004	0.004	0.044	0.044	0.0438	0.4375	26-week dog feeding study
7	**Acetone (67-64-1)**	1187	100	0.875	0.875	8.750	0.001	0.0007	0.0074	rat oral subchronic study
8	**Acetophenone (98-86-2)**	49.1	423	1.234	3.701	12.338	0.025	0.0754	0.2513	Rat Oral Subchronic Study
9	**Acrolein (107-02-8)**	0.23	0.05	0.004	0.004	0.044	0.019	0.0190	0.1902	Chronic Gavage Rat
10	**Acrylamide (79-06-1)**	0.03	0.2	0.002	0.002	0.175	0.058	0.0583	5.8333	Rat subchronic Drinking water study
11	**Acrylic Acid (79-10-7)**	5.89	53	4.638	0.464	4.638	0.787	0.0787	0.7874	Rat reproductive study
12	**Aldrin (309-00-2)**	0.25	0.025	0.000	0.000	0.002	0.001	0.0009	0.0088	Rat Chronic feeding study
13	**Allyl Alcohol (107-18-6)**	1.19	4.8	0.042	0.420	0.420	0.035	0.3529	0.3529	Subchronic oral rat study (drinking water)
14	**Ammonia Sulfamate (7773-06-0)**	10	214.3	1.875	1875.125	1875.125	0.188	187.5125	187.5125	90-day rat feeding study
15	**Antimony (7440-36-0)**	0.5	0.35	0.003	0.031	0.306	0.006	0.0613	0.6125	Rat chronic oral bioassay
16	**Arsenic (7440-38-2)**	0.01	0.0008	0.002	0.000	0.001	0.233	0.0070	0.0700	Human Chronic oral exposure
17	**Atrazine (1912-24-9)**	5	3.5	0.306	3.063	30.625	0.061	0.6125	6.1250	2-year rat feeding study
18	**Atrazine (1912-24-9)**	5	4.97	0.435	0.043	43.488	0.087	0.0087	8.6975	1-year dog feeding study
19	**Barium (7440-39-3)**	0.5	0.21	0.613	0.018	1.838	1.225	0.0368	3.6750	Subchronic human study / community exposure study
20	**Barium (7440-39-3)**	0.5	65	189.583	5.688	5.688	379.167	11.3750	11.3750	Subchronic rat study

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21	**Barium (7440-39-3)**	0.5	45	131.250	3.938	13.125	262.500	7.8750	26.2500	Chronic rat study
22	**Benomyl (17804-35-2)**	10	5	0.438	0.438	0.438	0.044	0.0438	0.0438	13- Generation Reproduction Rat Study
23	**Benzene (71-43-2)**	1.6	1.2	0.035	0.105	0.350	0.022	0.0656	0.2188	Human Occupational Study
24	**Beryllium (7440-41-7)**	0.002	0.46	0.013	0.403	4.025	6.708	201.2500	2012.5000	Dog dietary Study
25	**Biphenyl (92-52-4)**	1.3	50	4.375	4.375	43.750	3.365	3.3654	33.6538	Rat Chronic oral study
26	**Bromoform (75-25-2)**	5.17	17.9	0.157	0.157	1.566	0.030	0.0303	0.3029	Rat subchronic oral gavage bioassay
27	**Cadmium (7440-43-9)**	0.01	0.005	0.004	0.000	0.004	0.438	0.0438	0.4375	Human Studies involving chronic exposure
28	**Cadmium (7440-43-9)**	0.01	0.01	0.009	0.001	0.001	0.875	0.0875	0.0875	Human Studies involving chronic exposure
29	**Calcium Cyanide (592-01-8)**	5	19.1	1.671	1.671	16.713	0.334	0.3343	3.3425	Rat Chronic Oral Study
30	**Caprolactam (105-60-2)**	5	50	4.375	4.375	43.750	0.875	0.8750	8.7500	rat oral three generation reproduction study
31	**Captafol (2425-06-1)**	0.1	2	0.018	0.175	1.750	0.175	1.7500	17.5000	1-yr dog feeding study
32	**Captan (133-06-2)**	5	12.5	1.094	1.094	10.938	0.219	0.2188	2.1875	1 generation and 3 generation rat reproductive studies
33	**Carbaryl (63-25-2)**	5	9.6	0.840	0.084	0.840	0.168	0.0168	0.1680	Rat Chronic feeding study
34	**Carbofuran (1563-66-2)**	0.1	0.5	0.044	0.044	0.438	0.438	0.4375	4.3750	1-yr dog feeding study
35	**Carbon Disulfide (75-15-0)**	31.1	11	0.963	0.963	9.625	0.031	0.0309	0.3095	Rabbit inhalation teratogenic study
36	**Carbon Tetrachloride (56-23-5)**	31.5	0.71	0.006	0.006	0.062	0.000	0.0002	0.0020	Subchronic rat gavage study
37	**Chlorine (7782-50-5)**	1.45	14.4	1.260	12.600	126.000	0.869	8.6897	86.8966	Rat Chronic Drinking water study
38	**Chlorine dioxide (10049-04-4)**	0.28	3	0.263	2.625	2.625	0.938	9.3750	9.3750	

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39	**Chlorobenzene (108-90-7)**	46	19	0.166	0.166	1.663	0.004	0.0036	0.0361	13-week dog study oral exposure
40	**Chloroform (67-66-3)**	48.8	12.9	0.113	1.129	11.288	0.002	0.0231	0.2313	Dog chronic oral bioassay
41	**Chlorpyrifos (2921-88-2)**	0.1	0.03	0.026	0.000	0.026	0.263	0.0026	0.2625	120 day human cholinesterase inhibition study
42	**Chromium III Insoluble salts (16065-83-1)**	0.01	0.1	0.009	0.009	0.088	0.875	0.8750	8.7500	Rat Chronic feeding study
43	**Cumene (98-82-8)**	245.8	110	0.963	9.625	96.250	0.004	0.0392	0.3916	Rat oral gavage study
44	**Cyanogen (460-19-5)**	21.3	21.6	1.890	1.890	18.900	0.089	0.0887	0.8873	Rat Chronic oral study
45	**Cyclohexanone (108-94-1)**	80.3	462	40.425	40.425	404.250	0.503	0.5034	5.0342	Rat chronic oral study
46	**Cyclohexylamine (108-91-8)**	40.6	18	1.575	0.158	1.575	0.039	0.0039	0.0388	Rat chronic oral study
47	**DDT (50-29-3)**	1	0.05	0.004	0.004	0.044	0.004	0.0044	0.0438	27-week rat feeding study
48	**Demeton (8065-48-3)**	0.05	0.04	0.000	0.004	0.035	0.007	0.0700	0.7000	12-yr feeding in rats
49	**Di(2-ethyl hexyl) phthalate (117-81-7) DEHP**	5	19	0.166	1.663	16.625	0.033	0.3325	3.3250	Guinea pig subchronic to chronic oral bioassay
50	**Dibutyl phthalate (84-74-2)**	5	125	1.094	10.938	109.375	0.219	2.1875	21.8750	Rat subchronic to chronic, oral bioassay
51	**Dichlorodifluoromethane (75-71-8)**	4047.9	15	1.313	1.313	13.125	0.000	0.0003	0.0032	Rat chronic oral study
52	**Dichloromethane (75-09-2)**	173.7	5.85	0.512	0.512	5.119	0.003	0.0029	0.0295	2-yr rat drinking water bioassay
53	**Dichlorvos (62-73-7)**	0.1	0.05	0.004	0.004	0.044	0.044	0.0438	0.4375	1-yr dog feeding study
54	**Dieldrin (60-57-1)**	0.25	0.05	0.004	0.004	0.044	0.018	0.0175	0.1750	2-yr rat feeding study
55	**Diethylphthalate (84-66-2)**	5	750	6.563	65.625	656.250	1.313	13.1250	131.2500	Rat Subchronic oral feeding study
56	**Diphenylamine (122-39-4)**	10	2.5	0.219	2.188	2.188	0.022	0.2188	0.2188	2-yr dog study

NO	Chemical Name	TLV (mg/m^3)	Chosen Study Factor	Interim OEV Air Conc. from IRIS	OEV from ADJ	OEV from MOD	Ratio IRIS OEV/TLV	Ratio ADJ OEV/ TLV	Ratio Mod OEV/TLV	Study
57	**Diquat (2764-72-9)**	0.5	0.22	0.019	0.002	0.019	0.039	0.0039	0.0385	Chronic rat study (dietary)
58	**Disulfoton (298-04-4)**	0.05	0.04	0.000	0.000	0.004	0.007	0.0070	0.0700	2-yr rat study oral exposure
59	**Diuron (330-54-1)**	10	0.625	0.018	0.005	0.055	0.002	0.0005	0.0055	2-year dog feeding study
60	**Endosulfan (115-29-7)**	0.1	2.9	0.254	0.254	2.538	2.538	2.5375	25.3750	2-year rat feeding study
61	**Endosulfan (115-29-7)**	0.1	0.57	0.050	0.050	0.499	0.499	0.4988	4.9875	1-year dog feeding study
62	**Endrin (72-20-8)**	0.1	0.025	0.002	0.022	0.219	0.022	0.2188	2.1875	Dog chronic bioassay
63	**Ethion (563-12-2)**	0.05	0.05	0.004	0.004	0.044	0.088	0.0875	0.8750	Dog chronic bioassay
64	**Ethyl Acetate (141-78-6)**	1441.3	900	7.875	78.750	787.500	0.005	0.0546	0.5464	Rat oral subchronic study
65	**Ethyl benzene (100-41-4)**	434.2	97.1	0.850	8.496	84.963	0.002	0.0196	0.1957	Rat subchronic to chronic oral bioassay
66	**Ethyl ether (60-29-7)**	1212.6	500	1.458	4.375	43.750	0.001	0.0036	0.0361	Rat oral subchronic study
67	**Ethylene glycol (107-21-1)**	100	200	17.500	17.500	175.000	0.175	0.1750	1.7500	Chronic rat oral feeding study
68	**Fenamiphos (22224-92-6)**	0.1	0.025	0.002	0.000	0.002	0.022	0.0022	0.0219	2-year feeding dog study
69	**Fluorine (7782-41-4)**	1.55	0.06	0.525	0.005	0.053	0.339	0.0034	0.0339	Epidemiological studies in children
70	**Fonofos (944-22-9)**	0.1	0.2	0.018	0.002	0.018	0.175	0.0175	0.1750	2-year dog study
71	**Formaldehyde (50-00-0)**	0.37	15	1.313	0.131	1.313	3.547	0.3547	3.5473	2-4 yr bioassay
72	**Furfural (98-01-1)**	7.86	7.9	0.023	0.691	6.913	0.003	0.0879	0.8795	Rat oral subchronic study
73	**Heptachlor (76-44-8)**	0.05	0.15	0.004	0.001	0.013	0.088	0.0263	0.2625	2-year rat feeding study
74	**Heptachlor epoxide (1024-57-3)**	0.05	0.0125	0.000	0.000	0.001	0.002	0.0022	0.0219	60-week dog feeding study
75	**Hexachlorobenzene (118-74-1)**	0.002	0.08	0.007	0.001	0.007	3.500	0.3500	3.5000	Rat chronic feeding study
76	**Hexachlorocyclopentadiene (77-47-4)**	0.11	7	0.061	0.061	0.613	0.557	0.5568	5.5682	Rat subchronic oral bioassay
77	**Hexachloroethane (67-72-1)**	9.7	1	0.009	0.088	0.875	0.001	0.0090	0.0902	Rat subchronic dietaty study
78	**Hydrogen Cyanide (74-90-8)**	5.2	11.2	0.980	9.800	98.000	0.188	1.8846	18.8462	Rat Chronic Oral Study

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79	**Hydrogen sulfide (7783-06-4)**	13.94	3.1	0.027	0.271	2.713	0.002	0.0195	0.1946	Pig oral toxicity study (Subchronic)
80	**Isobutyl alcohol (78-83-1)**	151.6	316	2.765	27.650	276.500	0.018	0.1824	1.8239	Rat oral subchronic study
81	**Isophorone (78-59-1)**	28.3	15	0.131	13.125	131.250	0.005	0.4638	4.6378	90-day dog feeding study
82	**Malathion (121-75-5)**	1	0.23	0.201	0.002	0.020	0.201	0.0020	0.0201	Subchronic human feeding study
83	**Maleic anhydride (108-31-6)**	0.4	10	0.875	0.875	0.875	2.188	2.1875	2.1875	Rat oral chronic study
84	**Manganese (7439-96-5)**	0.2	0.14	1.225	0.001	0.012	6.125	0.0061	0.0613	Human Chronic Ingestion Data
85	**m-dinitrobenzene (99-65-0)**	1.03	0.4	0.001	0.035	0.350	0.001	0.0340	0.3398	rat subchronic oral study
86	**Methanol (67-56-1)**	262	500	4.375	4.375	43.750	0.017	0.0167	0.1670	Rat oral subchronic study
87	**Methomyl (16752-77-5)**	2.5	2.5	0.219	0.219	2.188	0.088	0.0875	0.8750	2-year dog feeding study
88	**Methoxychlor (72-43-5)**	10	5.01	0.044	0.438	4.384	0.004	0.0438	0.4384	Rabbit teratology study
89	**Methyl ethyl ketone (78-93-3)**	589.8	1771	5.165	1549.625	15496.250	0.009	2.6274	26.2737	Multigeneration/ Developemental Rat feeding study
90	**Methyl methacrylate (80-62-6)**	205	136	11.900	1.190	11.900	0.058	0.0058	0.0580	Rat drinking water study
91	**Methyl parathion (298-00-0)**	0.2	0.025	0.002	0.000	0.002	0.011	0.0011	0.0109	2 year rat feeding study
92	**Metribuzin (20187-64-9)**	5	2.5	0.219	0.219	2.188	0.044	0.0438	0.4375	2-year feeding study in dogs
93	**Molybdenum (7439-98-7)**	10	0.14	0.041	0.001	0.012	0.004	0.0001	0.0012	Human 6-year to lifetime dietaty exposure study
94	**m-Phenylenediamine (108-45-2)**	0.1	18	0.158	0.158	1.575	1.575	1.5750	15.7500	Rat oral subchronic
95	**N,N-Dimethylaniline (121-69-7)**	24.8	22.32	0.020	1.953	6.510	0.001	0.0788	0.2625	Mouse bioassay gavage bioassay
96	**Naled (300-76-5)**	0.1	0.2	0.018	0.002	0.018	0.175	0.0175	0.1750	2-year rat Study, Dietary
97	**Naphthalene (91-20-3)**	52.4	71	0.207	0.621	6.213	0.004	0.0119	0.1186	Subchronic oral rat study

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98	**n-Butanol (71-36-3)**	60.6	125	1.094	10.938	109.375	0.018	0.1805	1.8049	Rat oral subchronic study
99	**Nickle Soluble Salts**	0.1	5	0.146	0.438	4.375	1.458	4.3750	43.7500	Subchronic oral rat study
100	**Nitrobenzene (98-95-3)**	5.04	4.6	0.004	0.403	4.025	0.001	0.0799	0.7986	Rat/Mouse subchronic inhalation study
101	**o-Chlorotoluene (95-49-8)**	258.9	20	0.175	1.750	17.500	0.001	0.0068	0.0676	15-week rat oral exposure study (gavage)
102	**o-Dichlorobenzene (95-50-1)**	150.3	85.7	0.750	7.499	74.988	0.005	0.0499	0.4989	2 year rat study, oral exposures
103	**Paraquat (4685-14-7)**	0.5	0.45	0.039	0.039	0.394	0.079	0.0788	0.7875	1-year dog feeding study
104	**Pentachloronitrobenzene (82-68-8)**	0.5	0.75	0.022	0.066	0.656	0.044	0.1313	1.3125	2-year dog feeding study
105	**Pentachlorophenol (87-86-5)**	0.5	3	0.263	0.026	0.263	0.525	0.0525	0.5250	Rat oral chronic study
106	**Phenol (108-95-2)**	19.25	60	5.250	5.250	52.500	0.273	0.2727	2.7273	Rat oral developemental study
107	**Phosphine (7803-51-2)**	1.4	0.026	0.002	0.000	0.002	0.002	0.0002	0.0016	Rat oral chronic study
108	**Phthalic anhydride (85-44-9)**	6.06	1562	13.668	13.668	136.675	2.255	2.2554	22.5536	Chronic mouse oral study
109	**Picloram (1918-02-1)**	10	7	0.613	0.061	0.613	0.061	0.0061	0.0613	6-month dog feeding study
110	**Potassium cyanide (151-50-8)**	5	27	2.363	2.363	23.625	0.473	0.4725	4.7250	Rat Chronic Oral Study
111	**Propargyl alcohol (107-19-7)**	2.3	5	0.015	4.375	43.750	0.006	1.9022	19.0217	Rat oral subchronic study
112	**Pyridine (110-86-1)**	16.2	1	0.009	8.750	8.750	0.001	0.5401	0.5401	90-day rat oral gavage study
113	**Rotenone (83-79-4)**	5	0.38	0.033	0.003	0.033	0.007	0.0007	0.0067	2-Generation Reproduction Study
114	**Selenium (7782-49-2)**	0.2	0.015	0.044	0.001	0.013	0.219	0.0066	0.0656	Human and epidemiological study
115	**Silver (7440-224)**	0.1	0.014	0.041	0.000	0.001	0.408	0.0012	0.0123	2 -9 year human I V study
116	**Sodium azide (26628-22-8)**	0.29	3.57	0.031	0.031	0.312	0.108	0.1077	1.0772	Rat oral subchronic study

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117	**Sodium cyanide (143-33-9)**	5	20.4	1.785	0.179	0.179	0.357	0.0357	0.0357	Rat Chronic Oral Study
118	**Sodium fluoroacetate (62-74-8)**	0.05	0.05	0.000	0.000	0.004	0.003	0.0088	0.0875	13-week rat oral study (gavage)
119	**Strychine (57-24-9)**	0.15	2.5	0.002	0.022	0.219	0.015	0.1458	1.4583	13-week rat oral study (gavage)
120	**Styrene,monomer (100-42-5)**	85.2	200	1.750	1.750	17.500	0.021	0.0205	0.2054	Dog subchronic oral study
121	**Tetrachloroethylene (127-18-4)**	169.5	14	0.123	1.225	12.250	0.001	0.0072	0.0723	6-week mouse gavage study
122	**Tetraethyl lead (78-00-2)**	0.1	0.0012	0.000	0.000	0.000	0.000	0.0001	0.0011	rat subchronic study
123	**Thiram (137-26-8)**	1	5	0.044	0.044	0.438	0.044	0.0438	0.4375	2-year rat feeding study
124	**Toluene (108-88-3)**	188.4	223	1.951	19.513	195.125	0.010	0.1036	1.0357	13-week rat gavage study
125	**trans-1,2-Dichloroethylene (156-60-5)**	793	17	0.149	1.488	14.875	0.000	0.0019	0.0188	90-day mouse drinking water
126	**Trichlorofluoromethane (75-69-4)**	5619	349	3.054	305.375	1017.917	0.001	0.0543	0.1812	Cancer bioassay studies in rats and mice
127	**Vanadium pentoxide (1314-62-1)**	0.05	0.89	0.078	0.779	7.788	1.558	15.5750	155.7500	Rat chronic oral study
128	**Vinyl Chloride (75-01-4)**	2.6	0.09	0.026	0.008	0.079	0.010	0.0030	0.0303	Rat Chronic feeding study
129	**Warfarin (81-81-2)**	0.1	0.029	0.003	0.003	0.025	0.025	0.0254	0.2538	Human clincal studies
130	**Xylene (1330-20-7)**	434.2	179	15.663	15.663	156.625	0.036	0.0361	0.3607	Chronic Rat Gavage studey

Table 3: Comparing Ratios using Different Studies and Uncertainty Factors[1]

Conversion Approach	Subchronic Animal Studies[3] % < 1	Chronic Animal Studies[3] % < 1	Human Studies[3] % < 1
OEV Converted from RfD UF	**88**	**92**	**85**
Adjusted UF [2]	**85**	**86**	**100**
Modified UF [3]	**62**	**67**	**92**

1 –130 chemicals were grouped into 3 subgroups based on the RfD studies used for comparison. A result less than 1 indicates a calculated OEV that is more conservative than the actual TLV and a result of greater than 1 indicates a less conservative value.

2 – Adjusted UF is using simple basic toxicology principles for setting a UF (i.e. if the study is chronic data UF =100, subchronic data UF= 1000, and if human data UF=10 or 1)

3 – Modified UF is using a UF that eliminated protection for sensitive populations (i.e. children and elderly) since OEVs are for the working population which is assumed to be healthy.

TABLE 4: New Chemicals that would allow for generation of an interim OEV				
Acenaphthene	Acenaphthylene	Acephate	Acetochlor	Acetyl chloride
Acifluoren, sodium	Alachlor	Alar	Aldicarb sulfone	Ally
Aluminum phosphide	Amdro	Ametryn	4-Aminopyridine	Amitraz
Ammonium acetate	Ammonium methacrylate	Anthracene	Apollo	Aramite
Aroclor 1016	Aroclor 1248	Aroclor 1254	Assure	Asulam
Avermectin B1	Azobenzene	Barium cyanide	Baygon	Bayleton
Baythroid	Benefin	Bentazon	Benzo[g,h,I]perylene	Benzo[k]fluoranthene
Benzoic Acid	Bidrin	Bis(2-chloroethoxy) methane	Bis(2-chloroisopropyl) ether	Bis(chloroethyl)ether
Bis(chloromethyl) ether	Bisphenol A.	Boron	Bromate	Brominated dibenzofurans
Bromochloromethane	Bromodichloromethane	p-Bromodiphenyl ehter	Bromomethane	Bromoxynil
Bromoxynil octanoate	Butyl benzyl phthalate	Butylate	t-Butylchloride	Butylphthalyl butylglycolate
Cacodylic acid	Carbonyl sulfide	Carbosulfan	Carboxin	Chloral hydrate
Chloramben	Chlorimuron-ethyl	Chlorine cyanide	Chlorite	p-Chloroaniline
Chlorobenzilate	1-Chlorobutane	2-Chlorobutane	Chlorocyclopentadiene	Beta-Chloronaphthalene
2-Chlorophenol	Chlorothalonil	Chlorpropham	Chlorsulfuron	Copper cyanide
Cyanide, free	Cyanogen Bromide	Cyhalothrin/Karate	Cypermethrin	Cyromazine
Dacthal	Dalapon	Danitol	Di(2-ethylhexyl)adipate	1,4-Dibromobenzene
Dicamba	P,p'-Dichlorodiphenyltrichloroethane	2,4-Dichlorophenol	4-(2,4-Dichlorophenoxy)butyric acid	2,4-Dichlorophenoxyacetic acid
2,3 – Dichloropropanol	Difenzoquat	Diflubenzuron	Diisopropyl methylphosphonate	Dimethipin
Dimethoate	2,4-Dimethylphenol	2,6-Dimethylphenol	3,4-Dimethylphenol	4,6-Dinitro-o-cyclohexyl phenol
2,4- Dinitrophenol	2,4-Dinotriotoluene	Dinoseb	Diphenamid	1,4-Dithiane
Dodine	Endothall	Ethephon	s-Ethyl dipropylthiocarbamate	Ethyl-p-nitrophenyl phenylphosphorothioate
Ethylene glycol monobutyl ether	Ethylene thiourea	Ethylphthalyl ethylglycolate	Express	Fluometuron
Fluoranthene	Fluorene	Fluridone	Flurprimidol	Flutolanil
Fluvalinate	Folpet	Fosetyl-al	Glufosinate-ammonium	Glycidaldehyde
Glyphosphate	Haloxyfop-methyl	Harmony	Hexabromobenzene	Gamma-Hexachlorocyclohexane
Hexachlorophene	Hexahydro-1,3,5-trinitro-1,3,5-triazine	Hexazinone	Imazalil	Imazaquin

Iprodione	**Isopropalin**	**Isopropyl methyl phosphonic acid**	**Isoxaben**	**Lactofen**
Linuron	**Londax**	**Maleic hydrazine**	**Maneb**	**Mepiquat chloride**
Mercuric chloride	**Merphos**	**Merphos oxide**	**Metalaxyl**	**Methacrylonitrile**
Methamidophos	**Methidathion**	**4-(2-Methyl-4-chlorophenoxy) butyric acid**	**2-(2-Methyl-4-chlorophenoxy) propionic acid**	**2-Methyl-4-chlorophenoxyacetic acid**
Methylene Diphenyl Diisocyanate	**Methylmercury**	**2-Methylphenol**	**3-Methylphenol**	**Metolachor**
Mirex	**Molinate**	**Monochloramine**	**Napropamide**	**Nitrate**
Nitrite	**Nitroguanidine**	**Norflurazon**	**NuStar**	**Octabromodiphenyl ether**
Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine	**Oryzalin**	**Oxadiazon**	**Oxamyl**	**Oxyfluorfen**
Paclobutrazol	**Pendimethalin**	**Pentabromodiphenyl ether**	**Pentachlorobenzene**	**Permethrin**
Phenmedipham	**Phenylmercuric acetate**	**Phosmet**	**Pirimiphos-methyl**	**Potassium silver cyanide**
Prochloraz	**Prometon**	**Prometryn**	**Pronamide**	**Propachlor**
Propanil	**Propargite**	**Propazine**	**Propham**	**Propiconazole**
Pursuit	**Pydrin**	**Pyrene**	**Quinalphos**	**Resmethrin**
Savey	**Selenious acid**	**Sethoxydim**	**Simazine**	**Sodium diethyldithiocarbamate**
Strontium	**Systhane**	**Tebuthiuron**	**Terbacil**	**Terbutryn**
1,2,4,5-Tetrachlorobenzene	**1,1,1,2-Tetrachloroethane**	**2,3,4,6-Tetrachlorophenol**	**Tetrachlorovinphos**	**Tetraethyldithiopyrophosphate**
Thiobencarb	**Thiophanate-methyl**	**Triallate**	**Triasulfuron**	**1,2,4-Tribromobenzene**
2(2,4,5-Trichlorophenoxy) propionic acid	**2,4,5-Trichlorophenoxyacetic acid**	**1,1,2-Trichloropropane**	**Tridiphane**	**Trifluralin**
1,3,5-Trinitrobenzene	**Uranium, soluble salts**	**Vernam**	**Vinclozolin**	**White phosphorus**
Zinc and compounds	**Zinc phosphide**	**Zineb**		

Figure 1: Conversion of Oral NOAEL to Interim OEV Air Concentration

$$\text{Interim OEV Air Concentration} = \frac{(\ \text{RFD}^{1}\ )\ \text{BW}}{\text{Breathing Rate}} \qquad \textit{Equation 1}^{(18)}$$

where:

OEV *= Occupational Exposure Value (mg/m^3)*

RFD = Reference Dose Concentration (NOAEL^1 / UF)

NOAEL *= No Observed Adverse Effect Level (mg/kg/day)*

UF *= Uncertainty Factor (unit less)*

BW *= Body Weight (70kg)*

Breathing Rate *= (1m^3/hr)(8hr/day)*

[1] RfD was primarily based on NOAEL values. These values were not available for all chemicals assessed from IRIS. Where NOAEL values were not available the lowest observed adverse effect level (LOAEL) or the lowest effect level (LEL) were used.

Figure 2: Calculation for converting Acetone from an oral RfD to an interim OEV air concentration.

$$\text{Interim OEV air concentration (mg/m}^3) = \frac{(100\ \text{mg/kg/day} / 1000)70\text{kg}}{(\text{m}^3/\text{hour})(8\text{hours/day})}$$

$$\text{Interim OEV air concentration} = \frac{(0.10\ \text{mg/kg/day})70\ \text{kg}}{8\ \text{m}^3} = \frac{7\ \text{mg}}{8\ \text{m}^3} = 0.88\ \text{mg/m}^3$$

where: ***RFD = Reference Dose Concentration (NOAEL^1 / UF)***

NOAEL = 100 mg/kg/day

UF = 1000 (based on UF provided by IRIS)

Figure 3: Conversion of units of ppm to mg/m^3

$$\text{TLV in } mg/m^3 = \frac{[\text{TLV (ppm)}][\text{MW (g)}]}{24.45} \qquad \textit{Equation 2}^{(13)}$$

where:

MW = molecular weight of substance (grams)

24.45 = molar volume of air in liters at normal temperature and pressure conditions (25C and 760 torr).[ACGIH, 2004]

Example of conversion using Acetone:

$$\text{TLV in } mg/m^3 = \frac{(500ppm)\ (58.05g)}{24.45} = 1187\ mg/m^3$$

Figure 4: Ratio Comparison of OEV converted from RfD study and Existing TLV.

$$\text{Ratio Comparison} = \frac{\text{OEV Converted from RfD}}{\text{Existing TLV}} \qquad \textit{Equation 3}$$

where:

OEV *= calculated occupational exposure value from IRIS Oral RfD for particular chemical*

TLV *= current occupational exposure value from ACGIH for particular chemical*

Example of ratio comparison using Acetone:

$$\text{Acetone Ratio Comparison Result} = \frac{0.88}{1187} = 0.00074$$

Figure 5: Acetone Ratio Comparison using different UF values.

Note: Acetone's toxicological study in the IRIS database is a rat oral subchronic study.

Step 1: Calculating Acetone's ORAL RfD to Interim OEV Air Concentration

Equation 1 – Using IRIS UF and ADJ UF of 1000

$$\text{Interim OEV } mg/m^3 = \frac{(100\ mg/kg/day / 1000)70kg}{(1m^3/hour)(8hours/day)}$$

$$mg/m^3 = \frac{(0.10\ mg/kg/day)70\ kg}{(1m^3/hour)(8hours/day)} = \frac{7\ mg}{8\ m^3} = 0.88\ mg/m^3$$

Equation 2 – Using MOD UF of 100 to generate interim OEV

$$\text{Interim OEV } mg/m^3 = \frac{(100\ mg/kg/day / 100)70kg}{(1m^3/hour)(8hours/day)}$$

$$mg/m^3 = \frac{(1.0\ mg/kg/day)70\ kg}{(1m^3/hour)(8hours/day)} = \frac{70\ mg}{8\ m^3} = 8.75\ mg/m^3$$

Step 2: Ratio Comparison of the Interim OEVs to Actual OEV for Acetone

IRIS UF - 0.88 / 1187 = 0.00074 1350 times more conservative
ADJ UF - 0.88 / 1187 = 0.00074 1350 times more conservative
MOD UF - 8.75 / 1187 = 0.0074 136 times more conservative

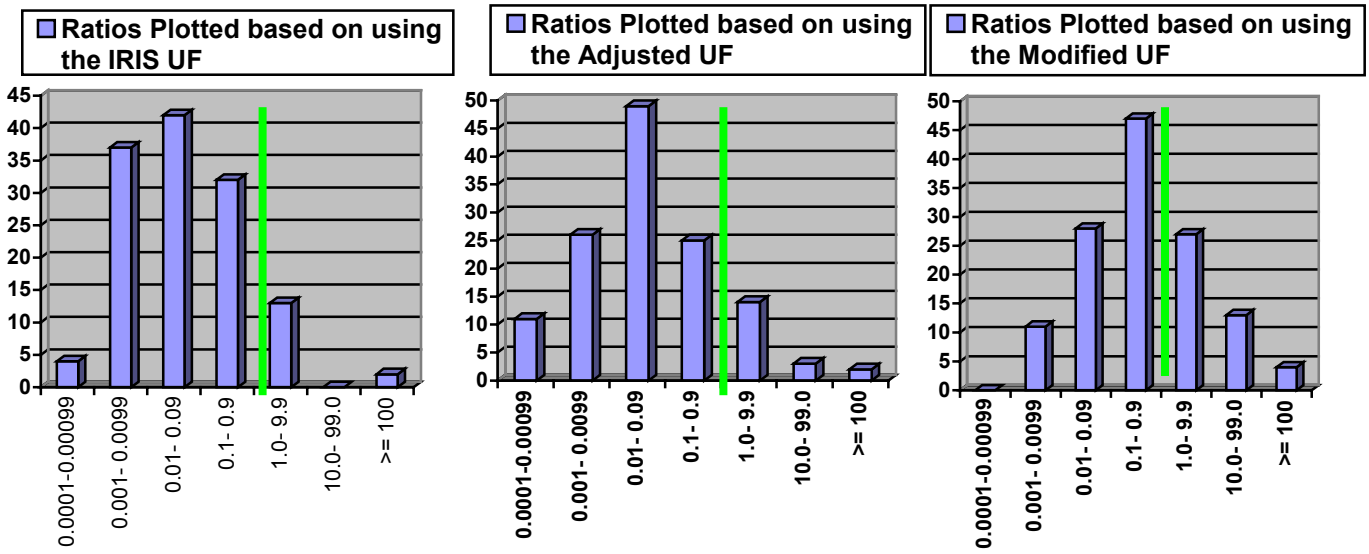

Figure 6: Distribution of the Ratio Results. The values to the left of the green line on each chart above were ratio results of less than one which resulted in more conservative interim OEVs calculated from the environmental data versus the current TLV.

CHAPTER 4

CONCLUSION

The use of the interim OEV approach is a required necessity for instances where no occupational exposure value is established or has been set by any state, federal, or scientific body. The calculations for developing the interim OEV are quite simplistic, and would quickly supply safety and industrial hygiene professionals with a reference for chemicals that do not currently have an established OEV. This process will help close the gap that exists in the area of occupational exposure limit development. It is not intended to replace the processes that currently exist through our various regulating bodies, like OSHA or ACGIH, but to supplement until permanent values are set. Given the overall conservative nature of the exposure values that are likely to be produced from the interim OEV approach, and the need for guidance values to more accurately access workers risk of exposure, the interim OEV approach is a useful mechanism in reducing risk and assessing exposure potentials.

There are estimated to be 70,000 chemicals used in industry today and currently there are only around 750 established OEVs, so the use of interim OEVs could have an enormous impact (1). Just using the IRIS database alone, there is the potential to have an additional 516 OEVs, which would increase the number of available OEVs for reference by about 68%. To determine the acceptability of developing interim OEVs from RfD study values, the interim OEVs were compared to established TLV values for 126 chemicals in EPA's IRIS database. This comparison indicated that the interim OEVs calculated are more conservative values than the existing TLV for 78% of the values based from sub-chronic studies, 80% for values based from chronic studies, and 90% of the values based from human studies (independent of the UF) (Table

3). For all values together, the interim OEVs calculated from RfD study values are more conservative 82% of the time. Therefore, the interim OEVs calculated are generally conservative enough for potential use as an acceptable surrogate exposure value for those chemicals that currently do not have an established exposure limit, such as the ACGIH TLV.

The interim OEV approach, which is developing a chemical's interim OEV from available environmental data for that chemical, used in this study is a simple process for establishing new OEVs, and current practices indicate that this approach is quite feasible. To be more specific, 24% of the TLVs established by ACGIH in 1968 were based on the process of analogy (2) and these were the values adopted by OSHA for the development of PELs, which are enforceable values (3,4). Analogy is establishing an exposure limit for a chemical based on that chemical's family toxicological data that is available and not on the individual chemical's toxicological data (2).

Currently, the EPA has a department that generates NCEL values which is another example that illustrates that the concept of interim OEVs is feasible. These values are developed and designed by the EPA to be interim OEVs for new chemicals being used in the US based on their available toxicological data until a permanent PEL is set for the new chemical (1).

Several recent studies have shown that environmental values, RfDs and RfCs, can be extrapolated from OEVs. These studies include the two EPC approach reports that Williams et al. completed (5,6). In one study, acceptable interim RfD and RfC values were proposed and in the other study, acceptable interim soil and water concentrations were developed from TLVs. Prior to the Williams group's work, in 1986 Calabrese was able to demonstrate that ambient air quality standards could be developed from TLVs that were more conservative than the present standards (7).

These studies listed above illustrate that a relationship exists between environmental and occupational values. So, if the practice of generating interim environmental values from occupational values is accepted and used as enforceable regulations in several states (5), completing the reverse is not far fetched and, like the interim environmental values, would provide substantial benefits. The key benefit would be providing safety and industrial hygiene professionals with data that would help them more accurately assess the overall risk to a worker.

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