Eighth Meeting of the Health Effects Advisory Committee (HEAC) for Permissible Exposure Limits for Airborne Contaminants in the Workplace California Code of Regulations, Title 8, Section 5155 September 4, 2018 Elihu Harris State Building, 1515 Clay Street Oakland, California

HEAC Members Present

Eric N. Brown, Dr PH, CIH, CSP, SCS Engineers (Industrial Hygiene)
Michael Bates, UC Berkley School of Public Health(Epidemiology)
Michael N. Cooper, MS, MPH, CIH, Principal Scientist, Mcooperconsulting LLC and UC Davis (Industrial Hygiene)
Will Forest, MPH, Santa Cruz County Department of Public Health (Epidemiology/Toxicology)
Robert Harrison, MD, MPH, School of Medicine, University of California, San Francisco (Occupational Medicine)
Sarah Janssen, MD, PhD, MPH, Occupational Medicine Department, Kaiser Permanente (Occupational Medicine)
Kent E. Pinkerton, PhD, UC Davis (pathology/inhalation Toxicology)
Howard Spielman, Health Sciences Associates and California Industrial Hygiene Council (Industrial Hygiene)
Mark Stelljes, PhD, SLR International Corporation (Toxicology)

Public and Interested Parties Present

Dan Leacox, Leacox and Associates
Bob Nocco, Chevron
Kashyap Thakore, California Department of Public Health, HESIS
Lindsay Stovall, American Chemical Council
Natalie Rainer, KH Law
Lisa Bailey, Gradient Corporation
Greg McClelland, Western Steel Counsel
Russell Johnson, ABC
Mark Pittser, ABC
Russ McCrary, CIEC/DCIW
Hank McDermott
Len Welsh
Michael Geyer, KERNTEC Industries
Steve Rank
Jim Kegebein, Kegebein Construction
Conrad Banez
Kevin Buchon
Manda Yanez, ABC
David Nunley, ABC
Elizabeth Traenor, Phylmar Group
Barbara Materna, CDPH
Elisa Koski, Occupational Safety and Health Standards Board

Division of Occupational Safety & Health

Garrett Keating, Chris Kirkham, Eric Berg, Kevin Graulich, Keummi Park and Mike Horowitz

DETAILED MINUTES

Below are detailed notes of the advisory meeting. These notes do not represent a transcript of the meeting, and are simply a summary of the notes taken by Cal/OSHA staff attending the meeting.

Chris Kirkham, opened the meeting, and explained the agenda and handouts. He introduced the staff and covered housekeeping items, and explained the HEAC process and scope. Kirkham then asked each committee member to identify themselves and their affiliations.

Kirkham, introduced the agenda and previewed the items on the agenda.

Mike Cooper, asked if the committee was going to re-visit how changes to the priority list occur.

Garrett Keating, indicated that today the intent was to adopt the 2018 list, not to consider new candidates. That would be a subject for an upcoming meeting.

Cooper, asked that the committee get a placeholder to talk about how chemicals get on the list and upgraded. There is still some confusion on this. **Keating** replied that the committee would.

Kirkham, continued general announcements, and then turned the meeting over for Keating to begin.

Keating, made an adjustment to the agenda and proposed to swap the order MIBK with the alcohols on the agenda. The acetates and alcohols have closely related toxicology issues so should be taken in sequence. Keating asked if there were any objections (none were noted).

Butyl Acetates – second review

The discussion included all four butyl acetates but focused mainly on issues related to the PBPK model for TBA and the adjustments and uncertainty factors used in the assessments. The basis for the PELs for sec- and n-butyl acetate and isobutyl acetate are based on irritation while the basis for tert-butyl acetate is cancer.

Keating, continued, describing the information on the white board where he presented the draft Cal/OSHA PEL recommendations. HEAC discussed the acetates at the last meeting, so he wanted to point out the changes since then. For acetate toxicology, health assessment is driven by n-butyl acetate and tert-butyl acetate because there is very little animal or human data on iso- or sec-butyl. He stated that the HEAC recommendation is in parallel with ACGIH - 50 ppm TLV/150 ppm STEL with the endpoint of irritation based largely on human studies. One addition to this current draft is a discussion of the conversion of the acetates into the alcohols to assess whether the 50 ppm PEL for the acetate would convert to a tissue concentration above the 20-ppm PEL for the alcohol. For example, if 50-ppm acetate converts to 50 ppm alcohol when the PEL is 20 ppm for alcohol, then toxicity may occur; however, that does not appear to be the case. In fact, only about 10% is converted by the olfactory region, so you would not anticipate the irritation.
Another change was regarding an animal study that found olfactory lesions in rats where the acetate converts to alcohol and acetic acid which may cause the irritation so we are not using that as an endpoint for this proposal.

There are no changes to the isobutyl or sec-butyl acetates from the previous draft.

The PEL for tert-butyl acetate (TBAC) is not based on the irritation endpoint like the other acetates. EPA and OEHHA have characterized TBAC as an animal carcinogen and possible human carcinogen. So DOSH reviewed both cancer and non-cancer (kidney damage) endpoints in the evaluation. Cancer endpoint leads to a value of 1 ppm, kidney damage leads to a value of 5 ppm. At this point, the recommendation is to use the cancer endpoint of 1 ppm. There is no pharmacokinetic model for inhalation of TBA or TBAC, and a question was raised at the previous meeting about the extrapolation from the oral to inhalation route for PBPK modeling. There are other

chemicals (MTBE and ETBE) that are metabolized to TBA and were used by EPA for target tissue modeling for TBA inhalation. EPA ran inhalation and drinking water studies with MTBE and ETBE that generated similar TBA tissue doses (as determined by PBPK) and kidney damage as was observed in the oral TBA study. EPA concluded that the PBPK model for TBA inhalation could be used to estimate target tissue doses (blood levels) in the oral TBA study.

Cooper, stated he met with Richard Corley, consultant, who was doing modeling with EPA and the American Chemical Society to look at TBA. Corley was an initial developer of the TBA PBPK model. Cooper asked about adjusting the model for continuous exposure to exposure which is discontinuous, such as occupational exposure. Corey indicated that some of the software for the models to examine this issue are no longer supported but he could try to continue to run these models if requested by Cal/OSHA.

Keating, added that the inhalation exposures need to be time adjusted to 5 day and 8 hours/day from the 24/7. So in this case NOAELS were multiplied by 4. EPA does have a concern because they are not sure the PBPK model is linear at the higher doses and the simple adjustment may not be accurate. Since the TBAC PEL is based on a cancer endpoint for TBA this extrapolation is not an issue, but this question of non-linearity needs to be considered for other substances when PBPK model results are extrapolated from continuous to discontinuous exposure.

Mark Stelljes, posed a question about TBAC. HEAC is proposing a level that is 50Xs lower than anyone else at this time and can HEAC defend it. HEAC does not know the accuracy of the model, oral to inhalation, and the correction from continuous exposure, and it is "erring" on the conservative side of all of those to get to the value of 1 ppm. Perhaps if HEAC did not err on the conservative side of all of those, HEAC might be at a value of 10. HEAC is assigning uncertainty factors to get to the value of 1 and not sure if actual data would support that, or show it is being too conservative.

Keating, stated the conversion for the cancer model is not the same as the one discussed above.

Stelljes, commented he also does not see that just replacing an "iso" with a "tert" would make a 50 fold difference in risk so the more he looks at it, the less confident he is that HEAC is doing this the best way. But it may be the only way HEAC can do it.

Keating, asked if Kashyap Thakore, CDPH toxicologist, could explain the HESIS TBAC cancer risk calculations. **Thakore** explained the cancer slope factor derived from the TBA oral study and its adjustment in the PEL calculation.

Keating, stated that EPA did not use the cancer endpoint for TBA because it is too confounded by potential alpha-2-G effects. Nonetheless, EPA did consider TBA to be a carcinogen with an unknown mechanism. More of a policy decision than a scientific decision by EPA. OEHHA does characterize TBA as an animal carcinogen and derived a cancer slope factor from the animal data.

Stelljes, asked whether this is the linearized multi-stage model that was used for cancer modeling. Maybe a threshold-based model should have been used. He stated this is probably why HEAC is getting a number of 1 because it is assuming it is linear multi stage.

Bob Harrison, stated he had raised this question before about PELs based on cancer endpoints. HEAC recommends a PEL, but not a STEL. He asked if that was because the scientific studies are not there to assess the carcinogenicity of intermittent exposures. The animal studies are done with continuous exposure.

Keating, stated that the STELs are not based on a cancer endpoint. **Will Forest** indicated agreement, and said to

not look at cancer risk as an acute exposure.

Stelljes, suggested a discussion on the 1 vs. 50 to justify HEAC's position as to why so low. Expand the summary discussion to explain. **Cooper** asked if HEAC resolved the question of human carcinogenicity. Keating indicated it is a possible human (2B) carcinogen, based on sufficient animal data, but not sufficient human data.

Howard Spielman, commented regarding carcinogenicity in the workplace, and that this may not be the right forum to figure this out. NIOSH will do some of this work for HEAC if HEAC requests it. He recommended using NIOSH for that. Also not usually STELs for carcinogens, but he is aware of one exception; asbestos has 1 f/cc as a 30 minute STEL. He stated he is not really sure what the rational is for that and wondered if anyone knew.

Keating, opened the floor to public.

Michael Geyer, KERNTEC Industries, stated he supports bringing in NIOSH. He commented that he wondered what the current actual exposure is, not just predictive models.

Eric Brown, stated he disagreed. Most of what is done is based on models and animal studies and not sampling data. He asked about how often do HEAC proposes an exposure limit before sampling methods are available, and how much sampling was done for chrome VI before the PEL was changed. An entire field of protection was developed following the revision of the PELs. So HEAC has to base it on toxicology not on sampling data.

Spielman, indicated that HEAC doesn't just look at California data, NIOSH uses worldwide data. But agreed that people are not monitoring. HEAC asks for monitoring data for feasibility, but no one submits data because they are not doing the monitoring.

Keating, wrapped up TBA. He stated he will better explain the cancer justification and other comments.

Eric Brown, asked about TBA to TBOH stoichiometry and if it is a one to one ratio. **Keating** indicated that he would add that information into the summary. TBAC has a much longer half-life than the other acetates, which may be part of why it poses a greater risk.

Stelljes, indicated that the RfC calculations were confusing. He suggested that may be HEAC could simplify that section of the summary. **Keating** replied that that was done for olfactory and was a 6-hour study, so was an occupational RfC. May be able to clarify that.

Harrison, mentioned that tert butyl acetate has been under scrutiny for a number of years by the Cal-EPA and the Air Resources Board because it is a potential alternative to VOCs and chlorinated solvents and those agencies have determined that TBAC is not a safe alternative because of its carcinogenicity. So he stated he supports the 1 ppm not only based on the science, but also to discourage its use.

Butyl Alcohols – first review

The basis for the PEL for n-butanol is irritation while the basis for tert-butanol is cancer. Potential reproductive effects of n-butanol were considered not suitable for evaluation at this time.

Keating, regarding n-butanol, the recommendation is 20 ppm, which coincides with ACGIH. There is good exposure data on n-butanol, it was used widely in photo and tire industry. One study on hearing loss is obscure and an odd endpoint so not widely accepted as an endpoint. Animal data on rat performance (rotorod, mazes

etc.) was used in a draft IRIS assessment to generate a lower OEL. Human data from multiple occupational studies, broken down by key conclusions with effects of irritation at 40 or 20 and above and no effect below. This is the basis for ACGIH TLV. There are no up to date reports on this effect, but based on the consistency of those studies, 20 ppm is the recommended number. The animal study was Korsak, which shows statistically significant data on rat performance. This IRIS data is draft and is available, but has not been moved forward for consideration by reviewers. Page 11 shows the studies come up with about 19 ppm as the effective dose in rats to which an uncertainty factor of 1000 was applied, resulting in 19 ppb. This is completely unsubstantiated in the eye effects, and certainly no narcosis or neurological effects have been seen at that level in workers, so the human irritation data was used as the basis for the OEL that leads to 20 ppm. In the past, authoritative bodies cited CNS effects were the basis for solvent OELs (dizziness, nausea, motor control), and now irritation is often being considered for solvents, resulting in lower OELs
So the recommendation for n-butanol is 20 ppm. Finally, there is an error in the draft at the PEL table. HEAC had the Cal/OSHA PEL at 20 ppm which should be listed as 50, and is a ceiling. There is a corrected version, so make sure the one everyone is looking at is correct.

Stelljes, stated he had one question on the data base uncertainty factor usage. HEAC has so much data, not sure an uncertainty factor of 3 is needed here. Of course, that would make the HEAC number 60, and that might not be protective based on what HEAC just talked about; so he stated he was ok with the number, but not sure he could support that uncertainty factor of 3. **Keating** replied by backing up a little bit; that butanol was the subject of a major review by an office of the EPA, because in vitro it had some very similar effects as ethanol. Some developmental and neurological effects of n-butanol have been observed in vitro but others have concluded that the animal data is not sufficient at this time to assess the developmental effects in humans (see Bales reference in summary). He stated that brings up the question of how the committee uses uncertainty factors verses actual data. He asked about how robust a data set must be where HEAC would not need to not use an uncertainty factor.

Harrison, inquired why the summary of developmental and reproductive effects, that there was some suggestion of positive findings, but did not use those. **Keating** replied that those studies had very high doses, thousands of ppm, so high dose effects. **Harrison** said that he just wanted to make sure that HEAC is not missing a significant reproductive effect.

Cooper, asked about the missing data of the NIOSH REL. **Keating** replied that he would look into that and update.

Forest, asked if the committee looked at a skin notation, and that NIOSH does. **Keating** said he would look at it.

MIBK – final review

Questions were raised about using a small human study to set the STEL for MIBK, the validity of basing a STEL on reproductive effects, and the cancer risk of MIBK. An adjustment factor used to round down the PEL estimate was presented.

Eric Brown, asked if the **committee** could toss out the obscure studies that are in the summary. **Keating** indicated that even though some of the studies had very low subject numbers, there might still be some benefit to the data. Keating said he will improve the explanations of why some data is not used.

Cooper, indicated that HEAC rounded from 7.5 to 5. He asked why it was not 10. **Keating** stated that in this case studies show a higher blood:air partition coefficient in humans than rats. Typically, it's the other way around.

Rats have a higher partition coefficient than humans, so humans must be exposed to a higher concentration to achieve the equivalent tissue dose. **Keating** pointed to the Errata where studies indicate that for MIBK, humans have a higher blood:air coefficient than rats. This was used as the basis for rounding down to 5 ppm. Humans are more likely to absorb MIBK than rats, and HEAC is basing its studies on rats, so when HEAC does its calculation it adjusts down. This is a standard adjustment in NOELs and LOELs. **Keating** will re-write the summary to include this data and show the calculation with the additional information from the Errata.

Forest, expressed concern about the dismissal of the cancer risk. **Stelljes** stated that page 8 of the document points out that by protecting for the non-cancer endpoint, you are effectively protecting against cancer without having to look at cancer as a separate endpoint. It gave chloroform as an example of an IRIS assessment where that was done.

Forest, took issue with the statement about CPN (Chronic Peripheral Nephropathy) and indicated that it was not an accurate statement. He stated he believes it is a spurious argument and does not want to see it used. **Keating** indicated that he would review. MIBK will be coming back for additional discussion and will address questions raised today. **Stelljes said he** also wanted Keating to look at the different categories of gas and how volatility changes the coefficient.

Keating asked if anyone found the STEL argument convincing or had questions. **Harrison** expressed concern that HEAC is sending a message that it may be a reproductive hazard and one can only be exposed to 5 (or 10) ppm for 8 hours, but one can be exposed to 50 for 15 minutes. **Stelljes** indicated that the STEL number may not be supported. **Spielman** stated that historically STELs are set to protect against short-term effects, not chronic long-term effects. Maybe the PEL is low enough to protect without the need for a STEL. He stated if HEAC was going to keep a STEL, it should be for irritation, but it was hard to explain both rationales.

Keating, stated that HEAC would come back to clarify 5 and 10 and maybe no STEL. Clearly, MIBK is not final.

Sulfur Dioxide – discussion

More information on SO2 exposure and usage was requested.

Keating, discussed the background documents and that there is no PEL recommendation at this time. ACGIH went from a 2 PPM 8-hour TLV and 5 PPM STEL TLV to a STEL TLV of 0.25 ppm based on effects on asthmatics. There are also other endpoints with SO2 to be considered, reproductive and developmental. Keating reviewed the handouts tables, ranges considered, etc.

Kent Pinkerton, stated that most of this data is based on sulfur in coal. He asked whether there is a California source other than coal. **Keating** responded, that to his knowledge there was not, however, SO2 is used as a fumigant in the wine industry. Most of the current human data is from China. **Michael Bates** said that where SO2 is from coal there will be particulate as well, which may complicate the results.

Keating, indicated that SO2 is now on the Proposition 65 list as a reproductive hazard with a Maximum Allowable Daily Level (MADL) of 10,000 micrograms per day so from that, the committee can calculate a concentration at 8 hours. Another factor with SO2 is that asthma can be acquired by "gassing" (an acute exposure) to SO2. He explained that after so many gassings, a normal worker can acquire asthma. HEAC should consider that a low enough STEL or TLV may prevent these gassings.

Harrison, stated he believed that there may be significant data available if we look at environmental verses occupational exposures. He asked whether there workers exposed to SO2, or whether it more of an

environmental issue. **Keating** indicated that DOSH will look at usage to see if this substance warrants work at this time, or if the committee should consider tabling SO2 for a while.

Spielman, referred to table 2, and asked if the symptoms would show for workers with asthma, with this respiration rate, even without SO2 exposure.

Geyer, said SO2 the wine industry has no information on long-term chronic exposure, but short-term exposure from a tank release can lead to a permanent disability. He commented that he has a concern because the industry has low wage workers sulfuring barrels, or bubbling it in wine, and the industry does not seem to be very concerned about this exposure.

Spielman, recommended checking with CARB to see where SO2 exposure occurs in California.

Keating, stated that DPR provided data on SO2 incidents (maybe 100 reports). He stated he would look into that.

This ends the morning agenda.

LUNCH BREAK

Priority 1 List

The Priority 1 list was amended to include chemicals approved at the June HEAC meeting.

Keating, introduced the priority list. He mentioned that there were some new substances from the last meeting that were nominated to the Priority 1 list. So the P1 list has t-butanol, n-butanol, turpentine, SO2 benzophenone, and parachlorobenzotriflouride (PCBTF). He explained that DOSH may move diesel exhaust and wild fire smoke to a special committee. DOSH will be re-evaluating that and adding to the priority list at a future meeting probably in about 3 to 6 months.

Manganese - discussion

An extensive discussion followed a presentation on the feasibility and health effects analysis of the proposed PEL.

Chris Kirkham introduced Greg McClellan and Hank McDermott from the Western Steel Council to do a presentation to the committee regarding manganese and the committee's proposed PEL.

Greg McClellan, Executive Director of the Western Steel Council (WSC), thanked the committee for allowing them to present. He explained WSC was prepared to discuss some of the feasibility issues and felt that the committee should consider some new information and toxicity data as well as potential engineering controls. The WSC represents approximately 8 to 10 million man-hours per year of ironworkers. Manganese is an ingredient in steel and the amount of manganese in steel varies. He explained WSC has challenges due to strict earthquake requirements here in California. He explained that WSC was prepared to discuss feasibility and more on toxicity. He then introduced Hank McDermott to start the power point presentation.

Hank McDermott, said that he was on the Cal/OSHA Feasibility Advisory Committee in the past, was on the Standards Board for 5 years, was the chief industrial hygienist for Chevron, and has been a consultant for about the last 15 years.

McDermott, began to review the presentation. See the slides for details. Most of the slides concern what the data looks like, published studies, and other good studies dealing with outdoor welding on mild steel. Indoor welding is already covered by a Cal/OSHA standard that requires ventilation, outdoor welding is more difficult to ventilate or control. What WSC found is that welders are exposed way over what is being proposed which would require respirators for everyone. Another concern is the quality of welds need to be improved to meet new seismic requirements. Manganese is a critical metal in the ductility of the steel, so it cannot be easily removed. Ventilation is considered a solution to exposure, but too much ventilation may weaken the weld. So the concern is that the committee is focusing on health effects, and not really looking at the feasibility issues.

Spielman, asked about the sampling and whether it was under the helmet or out of the helmet.
McDermott, stated that NIOSH said that under the hood is best, outside of the hood could be higher or lower. He wants to show that this feasibility will not be easy. Low manganese welding products are not as compliant.

McClellan, stated that the Northridge earthquake changed the steel welding industry dramatically.

Pinkerton, asked if these numbers affect manganese only, or are mixed. **McClellan** replied that steel and consumables very typically have single digit percentages of manganese in the product.

Harrison, thanked the council for pulling this information together. He asked about the research and whether McDermott discovered any new protective measures or equipment that would be feasible.

Brown, replied that this technology already exists. This issue was dealt with stainless, chrome 6, etc. so he believes it is fully feasible.

Pinkerton, asked if they measured particle size.

McClellan, stated that PAPRs lead to visibility issues, heat issues, additional equipment adds additional risk. Stated that WSC is not here today to recommend specific PEL or control measures, just that they need much further discussion before moving forward on the PEL

Kirkham, asked why a tight fitting PAPR on the 2nd slide. **McDermott** replied that the loose fitting PAPRs have an APF of 25. **Kirkham** indicated that there are loose fitting PAPRs with an APF of 1000 on the market which include some type of shroud. Second question from Kirkham was about AWS limits on wind speed within the welding zone (Slide 3). He asked about the nature of the concern. **McDermott** replied that AWS requires that wind speed not exceed 264 and that added ventilation on top of CalOSHA's minimum face velocity of 100 fpm could easily reach the 264 in some areas directly in front of the trunk which would interfere with the shielding gas. Kirkham stated that he understands that concern, but we have been dealing with 100 fpm rates in indoor welding for many years so asked about why it was different.

Geyer, quality of weld on stainless in the dairy industry is very critical so often have to put up an enclosure to block wind, or in a shop they relocate the trunk to minimize air flow that might mess up the weld.

Harrison, asked why they focused on outdoor welding, and what the distinction is between indoor and outdoor welding.

McDermott, responded that a lot of the indoor welding is at fixed workstations that are easier to design controls

into, while outdoor welding tends to be larger jobs where you have to move around. Also there are currently regulations requiring 100 fpm in the welding zone for indoor welding operations, that is not currently the case in outdoor welding.

Spielman, asked whether any of the data considered whether the difference is type of welding, for example stick welding, inert gas, flux cord. **McDermott** indicated that they did not break it down that way, and didn't see significant differences.

Bates, noted that they were reporting means, but inquired if the median might be a better measure of the data.

Spielman, talking about feasibility, one of the issues is monitoring under the hood. He stated that is a feasibility question, and questioned the validity of the data and the consistency of under the hood data from one data set to another.

Kirkham, introduced Lisa Bailey, toxicologist with Gradient Consulting. Bailey began her PowerPoint presentation. See the slides for details. She explained that she wanted to present information about the available scientific evidence they have related to the toxicity of manganese in occupational settings. She then started her presentation with some background information on manganese. She said she wanted to make sure the committee understands that manganese is an essential nutrient in the body.

Stelljes, pointed out that the range in an individual may vary. Normal for one person might be toxic to another.

Spielman, asked if 0.1 mg/m3 considered partial size distribution, and **Bailey** said it was all respirable (PM2) in the model.

Pinkerton, asked if other parts of the brain were affected and whether it. What is the globus pallidus (GP)? **Bailey** stated that they did model other parts of the brain. It also models the olfactory pathways to the brain.

Bates, asked how much confidence there was in the model, and whether there are any measurements to confirm the predictions. **Bailey** responded that there are measurements in primate studies to validate the model. In human studies they looked at manganese tracer studies to estimate levels, they have manganese measurements in blood, you can't really get manganese measurements in brain, but the levels in the blood were comparable to the levels in the model.

Stelljes, pointed out that the study shows a very steep dose response curve, especially when the curve reaches around 1.

Harrison, mentioned that in the March 2018 summary by Keating, the table of data and recommendations showed that HESIS had a different conclusion than Bailey is showing on the Ramoju study. HESIS concluded that the 0.55 in the GP associated with a 10% extra risk of producing any adverse response in humans. **Bailey** stated that the problem with the 0.55 is that it is based on means, so it does not really capture the range within the population. She agreed that the 0.55 is a no effect level. **Stelljes** commented that 10% increase risk at 0.55 still puts it in the normal range, so the point of departure would likely be higher than that. **Harrison** asked if the HESIS summary indicating that the air concentration related to the 0.55 is 70 ug (or 0.07 mg), which is very close to what HEAC is proposing as the PEL. **Bailey** said that her concern is that the model is based on manganese sulfate not manganese oxide, so it can be confusing.

Bailey, returned to the presentation. She stated that all of the calculations used by ACGIH, OEHHA, and CAL/OSHA are all based on faulty/outdated analyses, on top of which a protection factor of 3 is added. Manganese particles in welding fumes are very small, so the question of bioavailability is a good one, but since

we have good data, we don't need uncertainty factors added on. **Bates** asked, since every study only has a certain number of subjects in it, whether an uncertainty factor needed for human variability. **Bailey** replied that that is something to consider. Typically the uncertainty factor (UF) for human variability would be 10, but since we have the pharmacokinetic model which inlcudes potentially sensitive populations, they found that the uncertainty factor should be as low as 1.25, so not as big an effect as one might think.

Pinkerton, raised concerns that these numbers are high. He questioned if they were for peak transient levels. There is a disconnect with those levels and the report of no effect. **Bailey** replied that these are TWA concentrations and ranged over several studies.

Bailey, continued with the presentation. From a review of 25 studies on welders with manganese exposure, they come up with an OEL of 140 ug/m^3 that did not lead to adverse neurological effects (see slides for discussion). They believe that the no effect range would be from about 140 up to about 200, so the possible NOEL range of 140 to 200. In conclusion there is no need for a UF since there are three good studies that show an OEL of 140 to 200 that show no adverse effects. There is non-human primate data to support that, and it provides an extra layer of understanding of what the normal levels are.

Harrison, stated that he is still confused as to why the 77 ug level is not a good figure to work with. As a doctor, he doesn't want to tell a patient that they have 10% more manganese in their GP than they should, and I can't tell them if that is going to increase their risk of memory loss or trouble concentrating as they age, so he would find that 10% unacceptable. **Bailey** pointed out that that was based on the manganese sulfate not the manganese oxide. The other thing is that the EPA looked at that 10% and said that that was equivalent to the no affect level. **Harrison** said he would look at it again, he is not sure he would be happy with the no effect level if one is looking at preventing long term brain injury, he would want to set the PEL further to the left on the curve because the consequences of being wrong are great.

Forest, asked about the claim that the effects are reversible. **Bailey** said it was based on studies that looked at welders or other manganese occupations, removed them from manganese exposure and then looked at the effects. **Keating** clarified that the 1999 Roels study showed that some of the effects went away, others did not. **Forest** commented that partially reversible is the same as partially irreversible.

Spielman, asked if there is justification for two standards-one respirable and one total. **Bailey** stated that welding fume is generally all respirable. So 140 to 200 would be fine for welding fume, for total it would be higher. **Cooper** asked if the recommendation was the NOAL at 140, what uncertainty factor would Bailey recommend. **Bailey** answered that the Taylor et al study indicated that the intra species UF would not be higher than about 1.25 based on looking at elderly people, iron deficiency and liver dysfunction.

Dan Leacox, Leacox and Associates, asked if Bailey could go over the comparison of the different TLVs. **Bailey** re-explained the slide with the occupational no effect levels table. The US EPA has benchmark dose software now that produces a number of dose response curves depending on the model. OEHHA and ATSDR used that software to derive their values from the same study. The difference was using 10% vs 5% increased risk. **Harrison** re-stated his concern that the NOEL is not low enough for a PEL when the risk is memory, concentration and personality challenges.

Cooper, asked if there was any bioavailability data between the sulfate vs oxide. **Bailey** said there probably a way to get that from the studies, but not off the top of her head. She did say that the studies show that the sulfate is the most bioavailable, the oxide are less soluble. **Keating** agreed that sulfate is more available, but may not really be the main issue with the small particle size that can get down in the lung. **Pinkerton** agreed that these particles are ultra-fine, nano-size particles that can easily cross into the blood. Also he was concerned with deposition in the nasal cavity because that could be a route for entry to the brain. **Bailey** mentioned a

study that modeled deposits in the nasal cavity from welding fume and found that there is likely to be very little transport.

Forest, thought it was important to point out that the BMDL is in a sense equivalent to the NOEL, but its worth noting that the NOEL is the no observed effects level. That does not mean a no effects level, it means that whatever effects there might be are too statistically small to be observable. When you calculate a 10% BMDL, you are saying that that is the level where you would expect 10% and that 10% might be a NOEL because it's statistically not observable, but that said, these are effects that matter, and you don't want to dismiss them.

Harrison, asked if there is any information on what happened when the ACGIH lowered the TLV to 0.02 mg/m^3 since 2013. He asked whether people are able to reach that, how are they working with it, are they ignoring it. **McDermott** indicated that he has not seen any papers on that issue.

Elizabeth Traenor, Phylmar Group, asked if there is a significant difference between the 0.2 and 0.14. **Bailey** used a slide to explain the range of no effects from the mean of 140 to the top of the range of no effects at 200.

Bates, asked about the number of participants in the Roels study. **Bailey** said in the area of 92-96.

Cooper, brought up the previous discussion about in pregnancy, manganese levels increase. **Bailey** said that a variation of the model looked at the mother, child, fetus, and adult male. The results were still within the range of normal.

Keating, said that we just received this presentation last week, and have not had time to review all the studies. To the point of the uncertainty factor, at several meetings, reasons were presented why welding fume might be more bioavailable, not to specific solubility or particle size, but in results comparing welders to smelters or battery workers, etc. looking at manganese in blood. Blood levels are not the target tissue, but can be quickly and easily determined in welders. These new technologies (MRI) are promising at showing manganese uptake, but these two new studies in the presentation are showing novel subclinical effects that are new but not as established yet as eye hand coordination, reaction time, the more common endpoints that are measured in welders. They are the gold standard with some of those being irreversible, certainly in the Roels study. HEAC may need to evaluate its uncertainty approach. HEAC is taking the 0.077 ug/m3 and applying the UF of 3 to it. DOSH can look at these new studies, and report back to the committee or take it under advisement as input. Justification needs to be improved for the uncertainty factor of 3, and the committee can discuss the feasibility and economic issues more.

McClellan, said they will provide some economic impact data.

Next meeting will be December 4th.

Meeting adjourned.