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HALEY & ALDRICH

MEMORANDUM

16 May 2013
File No. 00820-210

TO: Massachusetts Department of Environmental Protection
Bureau of Waste Site Cleanup, 6th Floor
One Winter Street
Boston, Massachusetts 02108

Attn: Elizabeth Callahan

FROM: Haley & Aldrich, Inc.

SUBJECT: Proposed Amendments to the Massachusetts Contingency Plan, 310 CMR 40.0000

Haley & Aldrich is pleased to submit the following comments and suggested changes to the MassDEP proposed amendments to the MCP. If the Department has any questions during the review of our responses, please direct questions to Marc Richards at 617-886-7420 or mrichards@haleyaldrich.com.

PERMIT/TIER CLASSIFICATION AND NUMERICAL RANKING SYSTEM

40.0510: Tier Classification Process

- (2) (g) "Tier I classification submittals shall also contain the following: (1) the tearsheets from the newspapers containing the public notice…"

  We suggest requiring that copy(ies) of the tearsheet(s) be submitted to DEP within 7 days of receiving a copy from the newspaper(s), instead of as part of the Tier Classification submittal.

40.0530: Reclassification of RPs, PRPs, or Other Persons During Response Actions

- (4) "…disposal site shall submit a revised Tier Classification Submittal."
  - Change Submittal to Form.

40.0560: Response Action Deadlines and Requirements for Tier Classified Disposal Sites

- (7) (b), 7(d), and 8(c).
    - We suggest changing from 45 days to "taking effect upon submission" or taking effect within 21-days.

40.0583: Department Reclassification of a Tier Classified Disposal Site

- (3)(b) "the nature and extent of danger to health, safety, public welfare and the environment posed by the disposal site"

Change to "the risk to health, safety, public welfare and the environment posed by the disposal site"

ACTIVITY AND USE LIMITATIONS

1. In a Note to Reviewers immediately before the proposed changes to Subpart J, the Department asked for comment on whether metes and bounds descriptions of parcels subject to AUL documents should be eliminated and perhaps a certification (perhaps by an owner?) substituted.

   We recommend that the requirement for a metes and bounds description (Exhibit A) remain a component of an AUL. Although mistakes may occur from time to time, it is appropriate for this information to be included in the AUL so that parties conducting real estate transactions will clearly understand the property boundaries. Putting the responsibility on owners or LSPs is not appropriate as they have no ability to properly describe and certify the information. Individuals who have the appropriate training to develop property descriptions should continue to do so as has been the case in the past.

2. The Department's proposal to eliminate the separate LSP Opinion as a part of an AUL will certainly avoid the inevitable errors in formatting and transcription which occur currently between the sections of the 1075 form and the LSP Opinion (Exhibit C). However simply transporting the content of the LSP Opinion to the fourth "Whereas" clause of the 1075 Form will result in 1075 forms with significant variations in length and formatting as LSPs attempt to summarize the required information into one section of the form.

   The information should be included in a reformatted Exhibit C, limited to the information required by new sections 40.1074(2)(e), 40.1074(2)(f) and 40.1074(2)(g). The 4th Whereas clause in the AUL Form can then simply refer the reader to "Exhibit C" as it currently does, and Exhibit C will be a streamlined, simplified attachment and not duplicative of other language in the AUL. This approach will be a better way of streamlining AUL preparation than requiring lengthy text to be inserted in a "Whereas" clause.

3. The proposed revision in 40.1074(5) is somewhat confusing. We suggest the new sentence at the end of 40.1074(5), and the same language be included in the Note on the first page of Form 1075, be rewritten as follows:

   "Within 30 days of recording or registering a deed for a property which is subject in whole or in part to Notice of Activity and Use Limitation, a copy of such deed shall be submitted to the Department. This obligation shall attach both to the grantor and the grantee on such deed, provided that submission of such copy to the Department by either the grantor or the grantee shall satisfy this obligation."

4. We applaud the Department for reducing the notice period to interest holders for AUL Amendments to 30 days from the current 45 days, consistent with other AUL placement notification requirements.

VAPOR INTRUSION AND CLOSURE

40.0006: Terminology, Definitions and Acronyms

- We suggest adding the following:
  - "Daycare or Child Care Center means a facility operated on a regular basis whether known as a daycare, child nursery, nursery school, kindergarten, child play school, progressive school, child development center, pre-school, or known under any other name, which receives children, not of common parentage, under seven years of age, or under 16 years of age if these children have special needs, for non-residential custody and care during part or all of the day separate from their parent(s). Daycare or Child Care Center shall not include: any part of a public school system; any part of a private organized educational system, unless the services of such a system are primarily limited to kindergarten, nursery or related pre-school services; a Sunday school conducted by a religious institution; a facility operated by a religious organization *or commercial business* where children are cared for during short periods of time while persons responsible for the children are attending religious services; a family child care home; an informal cooperative arrangement among neighbors or relatives; or the occasional care of children with or without compensation therefore."

    This clarifies that "babysitting" services associated with health clubs or retail spaces are not included in the definition of daycare or child care.

- Definition of "residential Dwelling"
  - We suggest adding "or a building under construction without a certificate of occupancy" After "The term does not mean a structure with transient use, such as a hotel or hospital"

40.0046: Application of Remedial additives

- (3) – Suggest clarifying the process on how approval is issued and within what timeframe.

40.0313: Releases Which Require Notification Within 72 Hours

- (5)(f) "…in the discharge of vapors into a School" Add occupied before School
- (5)(f)(1.) "…wall of the structure, and within ten feet…" Change and to or
- (5)(f)(4.) "…fieldstone or concrete foundation, significant…" …" Change concrete to masonry block.
- (5)(f)(4): "One or more volatile organic compounds exist…" Please clarify whether this is meant to apply to VOCs present at any concentration or only above a threshold, such as GW-2.

What if vapor mitigation system is already known to be in place? There does not appear to be any relief from having to report in this case.

40.0425: Immediate Response Action Status and Remedial Monitoring Reports

- (5) (a) (3.) "A description of a monitoring program designed to ensure the continued effective mitigation of site conditions; and"

  Change to "A description of a monitoring program designed to ensure the continued effective mitigation of a Critical Exposure Pathway; and"

40.0006: Terminology, Definitions and Acronyms

- (12) - Historic fill definition

  How is weathered defined?

  How do RCRA characteristic hazardous soils (TLCP issues) relate to this definition? TCLP lead issues frequently exist in fill soils. (d) currently appears to exclude soils with TCLP lead above 5 mg/L from the Historic Fill definition.

  We assume that the application of the Historic Fill definition is solely based on the presence of fill materials and not the actual concentration of contaminants associated with the fill (excluding PCBs). If that is the case, it may be useful to clarify this point in the definition.

  We suggest deleting (b) as this is very difficult, and perhaps impossible, to determine.

Overall Comment: The proposed complex nature of permitting and notification related to Active Exposure Elimination Measures will tend to push remedies towards passive systems and away from active systems

An Exposure Pathway Elimination Measure does not produce waste requiring management and disposal or recycling."

> Change to "…An Exposure Pathway Elimination Measure does not produce waste requiring management and disposal or recycling, with the exception of systems that may require water knock-out tanks or voluntarily include carbon treatment.

40.0701: Purpose and Scope

- *(4)* Comments:
    - We understand the intent of this revision, however we see this revision only really applying to TCE issues. For the TCE example with the lower toxicity values, it would appear that an Active Exposure Pathway Elimination Measure could not be used and another form of remediation must be employed.

40.0711: Purpose and Scope

- *(1)* Comments: Add "or a Release Abatement Measure (RAM) "
- (5) "… and the Department, immediately upon failure of the system."

  Comment: We suggest "immediately" be further defined along with more detail related to the mechanics of reporting, including, who at the Department, how notifications are made, and within what specific timeframe?

40.0712: Operation of Active Exposure Pathway Elimination Measures

- (2) "…with a sufficient margin of safety to account for planned and unplanned shut-down.

  Comment: We suggest "sufficient margin of safety" be further defined.

40.0720: Discontinuing Operation of Active Exposure Pathway Elimination Measures No Longer Required to Maintain a Permanent or Temporary Solution

- (1)(a)(2) - Comment: change "season" to "seasonal"

40.0752: Requirements for Active Exposure Pathway Elimination Measure Permit Applications

- (1)(c) and (d) – We feel these two provisions may be too difficult to effectively implement.

40.0761: Conditions Applicable to all Active Exposure Pathway Elimination Measure Permits

- (2) Clarify "30 days". See sections 40.0701(4) and 40.0711(5) with respect to other referenced timing. The references to "60 days" and "immediately" appear to be contradictory.

40.1012: Application of Activity and Use Limitation

- (c)(2) "the concentrations of OHM at the disposal site are consistent with Anthropogenic background levels"

  Change to: the OHM at the disposal site are consistent with Anthropogenic background.

Please add the following:

- "(3)(c)(5) at disposal sites where current indoor air data in existing buildings pose a condition of No Significant Risk of harm to human health for current or future receptors and a current CEP does not exist and either concentrations of OHM in groundwater exceed GW-2 or concentrations of OHM in sub-slab soil gas exceed sub-slab soil gas screening values."

  We believe that this scenario, where current indoor air poses no risk to current, or future users, including a hypothetical resident, but groundwater or soil gas concentrations may be elevated, should be included as a "condition" and not a situation that would require an AUL. In this scenario, the requirement would be to evaluate the vapor intrusion (VI) pathway if conditions at the existing building change, the existing building was renovated, or if a new building was constructed and does not necessarily limit any activities or uses. If the result of the evaluation concluded that VI would pose risk or a CEP under these changed conditions, then remedial actions may be necessary and the implementation of an AUL to limit some use or activity may be required

40.1040: Permanent Solutions

- (1)(d) Add "approach or achieve" and delete "as close to".

RISK ASSESSMENT AND MCP STANDARDS

Toxicity Information:

MassDEP has proposed to use the USEPA PPRTV as the reference dose (RfD) value(s) for vanadium. Method 1 standards and the MassDEP Short Forms have been revised accordingly. As documented in the memorandum prepared by Dr. Stephen Clough, PhD DABT in Attachment A of this comment letter, the USEPA PPRTV has inherent flaws in its derivation which, in turn, severely overestimate risk. Specifically:

- The study used as the basis of the PPRTV failed to report drinking water (the vehicle for vanadium sulfate) intakes in the study animals, so the doses could not be accurately reported from the study.
- The most sensitive effect found in the toxicity study was increased blood pressure, an effect that is opposite that which has been reported in humans who have taken vanadium as a dietary supplement or in medication.
- The PPRTV is derived using an uncertainty factor of 3000, which is unprecedented. A review of the RfDs for 10 metals that are classically defined as metabolic poisons (e.g. antimony, arsenic, cadmium, cyanide, mercury) showed that uncertainty factors ranged from 1 to 1000, and the corresponding RfDs are all higher (less conservative) than the chronic PPRTV for vanadium. The comparison of RfDs implies that vanadium is more toxic than all of the classic heavy metals. Vanadium and compounds are clearly on the opposite end of the spectrum (much less toxic), as they are being offered widely to the public as nutritional supplements and as a panacea for Type 2 diabetes mellitus.

As detailed in Attachment A to this comment letter, we are recommending an alternative RfD based on data provided by the National Research Council and supported by the toxicological data base for vanadium.

310 CMR 40.0993(5)

We suggest retaining the original language of this section. In reviewing the proposed revised text, we do not think that it is appropriate to include a hierarchy of toxicological data sources in the MCP document itself that leaves no room for professional judgment in reviewing or choosing toxicity values. The original language already gives preference to MassDEP-derived toxicity values, and references the types of values that can be used for risk assessment purposes. If MassDEP wishes to recommend a hierarchy of toxicological sources, we suggest that this information would be more appropriate in a risk assessment guidance document or a Technical Update.

310 CMR 40.0006

Add following definition:

> Carcinogenic means an oil or hazardous material (OHM) that has been identified by US EPA as a Class A, B, or C carcinogenic compound (prior to 2005) or as "Carcinogenic to Humans," "Likely to be Carcinogenic to Humans," or "Suggestive Evidence of Carcinogenic Potential" in the US EPA 2005 Cancer Guidelines.
>
> Adding this definition clarifies that USEPA's classification of carcinogenicity should be used to determine when to apply cancer toxicity data from the sources identified in 310 CMR 40.0993(5).

Edit the following two definitions:

> Carcinogenic Slope Factor (CSF, also cancer slope factor) means an estimate of the increased cancer risk from exposure to a carcinogenic oil or hazardous material (OHM), expressed as risk per unit dose of (mg OHM/kg-day).
>
> Unit Risk means the excess lifetime cancer risk (ELCR) estimated to result from continuous exposure to a carcinogenic oil or hazardous material (OHM) per concentration unit of 1 μg/m3 in air or 1 μg/liter in water.

Remove the definitions for MRL and PPRTV; these are no longer necessary if the hierarchy of data sources is not included.

310 CMR 40.0974(2) Table 2

The Department has derived a Method 1 S-1 Standard for lead of 200 mg/kg, which is based on the 95th percentile value in the "natural" background data set in the MassDEP Technical Update on background. The 200 mg/kg level is derived based on the same criteria applied to almost all other OHM in determining a Method 1 S-1 Standard, and thus is transparent in its origin.

MassDEP has identified 300 mg/kg as a secondary Method 1 S-1 Standard for lead that would demonstrate "No Significant Risk" for a Permanent Solution with Conditions, and conditions would include best management practices (BMPs) for non-commercial gardening. As stated by Department staff at a 5 April 2013 meeting to discuss the Method 1 Standards, the basis for this 300 mg/kg value as the secondary Standard is that this is the level of the current Method 1 S-1 Standard. Given this approach, we believe the use of 300 mg/kg as a secondary Standard is inappropriate.

Specifically, the 300 mg/kg Method 1 Standard currently promulgated is based on the "land application of sludge" limit, and is not a risk-based value. In addition, the 300 mg/kg value is associated with a residential land use direct contact hazard index of between 0.2 and 1.0, and therefore does not have a target risk basis that is consistent with other OHM.

Should MassDEP wish to present a secondary Method 1 S-1 Standard for lead, we suggest identifying an approach to deriving such a value that has toxicological and risk-based validity. One possible approach might be to consider using a level identified by the United States Environmental Protection Agency (USEPA) as being protective for residential land uses, which is 400 mg/kg. Typically, USEPA does not require clean-up of lead levels in soil at or below 400 mg/kg. We would consider the level of 400 mg/kg to better represent an appropriate residential clean-up goal for lead, and also be consistent with the "conditions" given by MassDEP (BMPs for gardening) as applicable to a secondary Method 1 S-1 Standard for lead. In addition, using levels identical to those identified by USEPA improves interagency consistency and reduces confusion from the members of public who may not understand the details and rationale behind the different levels promulgated by state and federal jurisdictions

AQUEOUS PHASE LIQUID AND SOURCE CONTROL

40.0006: Terminology, Definitions and Acronyms

NAPL definition – We suggest deleting "The existence of NAPL in the subsurface strata is indicated….." This definition should reference the LNAPL CSM and not be solely based on visual means.

Non-Stable NAPL – We suggest this definition should also reference the LNAPL CSM.

40.0313: Release Which Require Notification Within 72 hours

We suggest changing the 72 hour notification to 120 days.

40.0483: Content of Phase I Report

(1)(e)(5) – Revise to the following "information and details on the likely presence of NAPL".

The balance of the proposed revision should be deleted as extent of release is not part of a Phase I evaluation.

MISCELLANEOUS AND CROSS-REFERENCING

40.0005 (7) – We suggest the new regulations shall take effect 3 months from date of publication.

40.0046 (1)(c) – We suggest the proposed revisions be further clarified as to readability.

40.0049: Remedial Air Emissions

(6) – Delete "that utilize" and replace with "that require the use of". Some systems have off-gas controls added simply for conservatism (voluntarily) and not because VOC reduction is required.

PILOT TESTS AS IT RELATES TO RAM PLANS AND PHASE III/IV SUBMITTALS

Although not directly a part of the regulation changes, the proposal to combine the Phase III/IV reports together may have implications on Pilot Tests as they are currently defined in the MCP. The current definition of Pilot Test is:

> "Pilot Test means a test designed to acquire information on the anticipated performance of a remedial system. A Pilot Test shall be considered assessment if it is conducted and completed within 21 consecutive days, excluding time required for sample analyses, and involves only soil vapor, Nonaqueous Phase Liquid and/or groundwater extraction, otherwise it shall be considered remediation."

Since only Pilot Tests involving soil vapor, Nonaqueous Phase Liquid and/or groundwater extraction are considered assessment, then all other Pilot Tests are considered remediation and must be conducted under a RAM or, for those Pilot Tests that exceed the scope of a RAM, under a Phase III (for the current MCP). However, Pilot Tests for remedial technologies often exceed the scope of a RAM. The MCP States:

> 40.0442(2) Release Abatement Measures conducted in accordance with the provisions of 310 CMR 40.0442(1) may include, without limitation:
>
> (a) the excavation and off-site disposal of up to 500 cubic yards (cumulative, for the disposal site in question) of soil contaminated by oil and/or hazardous material at concentrations equal to or greater than applicable Reportable Concentrations, in conformance with 310 CMR 40.0030;
>
> (b)the excavation and on or off-site treatment, recycling or reuse of up to 1500 cubic yards (cumulative, for the disposal site in question) of soil contaminated by oil and/or hazardous material at concentrations equal to or greater than applicable Reportable Concentrations, in conformance with 310CMR40.0030;
>
> (c) *the initiation of passive or active NAPL recovery systems that discharge to a closed container, or groundwater recovery or treatment systems that discharge Remedial Wastewater and/or Remedial Additives in accordance with 310 CMR 40.0040 to a sewer system, POTW, Non-Publicly Owned Treatment Works, surface water body, or to the ground surface or subsurface and/or groundwater*; or
>
> (d) *the implementation of a soil vapor extraction system and/or groundwater sparging system, with appropriate off-gas treatment and controls, as described in 310 CMR 40.0049*.

Under the current MCP, this limitation on RAMs and Pilot Tests does not pose an issue since the Phase IV isn't due until one year after the Phase III, and you get the benefit of the Pilot Test conducted during Phase III to facilitate your Phase IV. Under the proposed regulations, the Phase III and IV are due at

the same time, and if your Pilot Test exceeds the scope of a RAM (such as a thermal, in-situ bio, or ISCO pilot test), then it cannot be conducted unless you submit a Phase III in advance of the Phase IV.

Haley & Aldrich suggests that the definition of Pilot Test should be redefined to allow for a broader range of technologies to be tested, or the limitations on RAMs should be revised to allow such Pilot Tests to be performed.

Attachment A:

Clough, Stephen D. PhD, DABT, Haley & Aldrich, Inc., Memorandum: Review of USEPA PPRTV for Vanadium and its Soluble Inorganic Compounds Other than Vanadium Pentoxide, 7 May 2013.

C:\Users\mrichards\Documents\Work\LSP Info\2013 Proposed MCP Changes\HAI MCP Comments F.docx

Attachment A

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MEMORANDUM

7 May 2013
File No. 0825-210

TO: Bureau of Waste Site Cleanup, 6th Floor
One Winter Street
Boston, Massachusetts 02108

ATTN: Elizabeth Callahan

FROM: Stephen r. Clough, PhD, DABT

SUBJECT: Review of USEPA PPRTV for
Vanadium and its Soluble Inorganic
Compounds Other than Vanadium Pentoxide

The purpose of this memo is to review and assess the scientific validity of the oral Reference Dose (RfD) that the USEPA developed in the document entitled "Provisional Peer-Reviewed Toxicity Values For Vanadium And Its Soluble Inorganic Compounds Other Than Vanadium Pentoxide". The document presents a fairly comprehensive review of both human and animal studies addressing any effects of oral administration of vanadium. The derivation of a "provisional" reference dose (RfD) is fundamentally flawed, however, because the authors a) pay little to no attention to the fact that vanadium is "practically nontoxic" to humans via the oral route with no reported "poisonings" or adverse effects following ingestion of even relatively high doses of the most soluble forms (e.g. vanadium sulfate). The derivation of provisional subchronic and chronic RfDs is also flawed because a daily dose (in mg/kg/day) cannot be directly estimated from the peer-reviewed study chosen (Boscolo et al., 1994) as the "point-of-departure".

Vanadium is considered an essential nutrient in some animals. For instance, vanadium is essential in the diets of chickens; a deficiency has an adverse affect on bones, feathers, and blood. In humans, classification of vanadium as an "essential nutrient" is still a topic of debate among various research groups. Some consider vanadium to be an ultratrace element, requiring dietary intake of only 20 ug per day. Much of the scientific community believes vanadium is essential element in the diet of mammals (though a mechanism has yet to be identified), as well as an effective therapeutic agent against diabetes and cancer. The PPRTV, however, does not use a weight-of-evidence approach, i.e. it essentially disregards a plethora of scientific studies in humans. The document primarily focuses on research in which an negative effect (usually subclinical: the authors seem to key in on subtle histopathology) was observed, then selecting the lowest possible "point-of-departure" and over applying conservative uncertainty factors.

Human Studies

Vanadium compounds are renowned for their potent ability to "mimic" insulin and clearly have the ability to decrease plasma glucose and provide a significant improvement in insulin sensitivity in Type 2 diabetic subjects (this effect is also seen in cell cultures). Vanadate restores tissue responsiveness to insulin and hepatic glycogen levels and activates new synthesis of key enzymes for carbohydrate metabolism. Many of these studies have used vanadyl sulfate, which is the *most soluble* form (and therefore the *most bioavailable* species) of the inorganic compound.

Acute, subchronic or chronic vanadium toxicity, via the oral exposure route, has not been observed in humans. Vanadyl sulfate is sold 'over the counter' as a dietary supplement and is often used by diabetics to reduce blood sugar and bodybuilders for the purported anabolic effect. It has a low bioavailability in the GI tract (<10%) but, once absorbed, is eliminated in the urine with a half-life of approximately 15–40 hours (Sabbioni & Moroni, 1983). A thorough scientific review of almost all of the clinical studies evaluating the efficacy of vanadyl sulfate administered to diabetics for the control of Type II diabetes did not reveal *any adverse effects* in volunteer subjects (Thompson and Orvig, 2004). Similar studies with people self-administering vanadium supplements for its anabolic effects only report aesthetic effects (e.g. green tongue or stool). That said, many web sites caution that mineral supplements can be cumulative so it is best to start out on a low dose and/or to take a 'break' in the supplement regimen.

The PPRTV cites four short-term human studies, all of which use doses that are hundreds of times the provisional RfD proposed by the USEPA. The only adverse effects observed in human studies are a) gastrointestinal upset (stomach ache or diarrhea, most likely because vanadyl sulfate is so poorly absorbed by the gut) and b) a discolored (green) tongue. It is thus difficult to see why such a low toxicity endpoint, based on a subclinical effect in a rodent, would be developed to protect humans who might be exposed to vanadium at a hazardous waste site, when it is already known that vanadium has never been reported to cause *any* toxic effects in the general population.

It is interesting to note that, although the PPRTV's "are derived after a review of the relevant scientific literature", the document ignores a critical reference published by the National Research Council (2000) that derived safe dietary intakes for "essential" elements, which included vanadium. Their chapter on vanadium states that:

> "Vanadium in the forms of vanadyl sulfate (100 mg/day) and sodium metavanadate (125 mg/day) has been used as a supplement for diabetic patients. Although insulin requirements were decreased in patients with Type I diabetes, the doses of vanadium used in the supplements were about 100 times the usual intakes, and they greatly exceed the Tolerable Upper Intake Level (UL) for vanadium." [references removed]

Their derivation of a Tolerable Upper Intake Level is presented below under "*Evaluation of the Oral RfD*".

Animal Studies

Short term (subchronic) studies cited in the PPRTV document principally cover effects following oral exposure of mammals (mainly mice and rats) on a) hematology b) blood pressure and c) reproduction. Interpretation of short term studies is difficult because most of the studies examined few or no toxicological endpoints at doses of 10 mg V/kg-day or greater. Secondly, some of the subchronic studies may not be toxicologically viable in terms of usable data because many of the animals were artificially compromised, e.g. treated with streptozotocin to induce diabetes or uninephrectomized to induce hypertension. Finally, since the goals were not to define toxic endpoints, many had only one or two dose groups.

Most of the "toxic" effects appear to be marginal and usually consisted of a slight decrease in body weights compared to the control group. The LOAELs show a fairly consistent range from 3.0 mg/kg/day to 12 mg/kg/day, while the NOAELs ranged from 0.12 mg/kg/day (kidney histopathology) to 17 mg/kg/day. Taken together, however, it is difficult to identify if many of the measured responses are truly "toxic" endpoints because the intent(s) of the studies were mostly prophylactic in nature, i.e. could vanadium compounds *improve* a "disease" condition. It can be said, with a fair amount of confidence, that only the high dose levels showed any type of adverse toxicological effect on any animal/dose group. Taken as a whole, vanadium does not appear to target either the blood, blood forming organs or the reproductive system.

As presented in Table 10 in the PPRTV document, longer term chronic studies were not designed to identify frank or clinical adverse effects but principally to address either positive effects on diabetic rats or the potential for carcinogenicity. Lifetime studies by Kanisawa and Schroeder (1967) and Schroeder et al. (1970; 1975) did not identify any toxic effects nor production of any cancerous lesions. Even though these studies identified positive effects (increased body weight in treated males and increased life span and longevity in treated males and females), the PPRTV authors discount them as viable studies to derive an RfD because "histological evaluations performed in this study were not adequate to detect any but the most severe lesions" or "limitations in the histological evaluations performed in this study preclude the identification of effect levels from these data". A one year study conducted by Steffen et al. (1981) found a LOAEL for increased blood pressure (7 mg/kg/day) that was very similar to that of Dai et al. (1994) who found a LOAEL of 8 mg/kg/day (slight reduction in body weight).

Evaluation of the PPRTV Oral RfD

The PPRTV makes a brief mention of historical toxicity endpoints but does not elaborate on them. Because this reviewer believes past RfDs have a strong bearing on the critique of the current PPRTVs, they are reiterated as follows (obtained from the Risk Assessment Information System website):

<u>Vanadyl Sulfate</u>

- *Subchronic* Oral RfD: 0.01 mg/kg/day (ATSDR, 2012).
- Uncertainty Factor: 10 (human variability).
- NOAEL: 0.12 mg/kg/day (human), dietary supplement, 12 weeks.

- Principal Study: Fawcett et al., 1997

- Comments: Human subjects (12 men and 4 women) were administered capsules containing 0 (11 men and 4 women) or 0.5 mg/kg/day vanadyl sulfate trihydrate (0.12 mg vanadium/kg/day) for 12 weeks. Fasting blood samples were collected at 0 and 12 weeks and analyzed for hematological (erythrocyte count, hemoglobin, hematocrit, mean cell volume, mean cell hemoglobin, platelet count, and total and differential leukocyte count) and serum chemistry (cholesterol, high density lipoprotein, triglycerides, albumin, total protein, total and direct bilirubin, alkaline phosphatase, ALT) parameters. Body weight and blood pressure were measured at weeks 4, 8, and 12. No significant alterations in blood pressure, body weight, or hematological or clinical chemistry parameters were found.

Vanadyl Sulfate

- *Chronic* Oral RfD: 0.007 mg/kg/day (U.S. EPA, 1987, 1991a).

- Uncertainty Factor: 100 (inter- and intraspecies variability).

- NOAEL: 0.7 mg/kg/day (rat), drinking water, lifetime.

- Principal Study: Schroeder et al., 1970.

- Comments: The NOAEL is derived from a lifetime single exposure level study in which rats were exposed to 5 ppm V, as vanadyl sulfate, in drinking water. The only reported effects were minor changes in serum chemistry. The Uncertainty Factor of 100 is the product of a 10-fold uncertainty in extrapolating from laboratory animals to humans and a 10-fold uncertainty to protect sensitive individuals.

Sodium Metavanadate

- *Chronic* Oral RfD: 0.001 mg/kg/day (U.S. EPA, 1987, 1991a).

- Uncertainty Factor: 1000

- NOAEL: 1.32 mg/kg/day.

- Principal Study: Domingo et al., 1985.

- Comments: The NOAEL is derived from a study in which rats were given 0, 5, 10 and 50 ppm sodium metavanadate, in drinking water for 3 months. Impaired kidney function was seen at 50 ppm, and 10 ppm was considered a NOAEL. The Uncertainty Factor of 100 is the product of a 10-fold uncertainty in extrapolating from laboratory animals to humans, a 10-fold uncertainty to extrapolate from a subchronic to chronic exposure, and a 10-fold uncertainty to protect sensitive individuals.

Vanadyl Sulfate

- *Chronic* Tolerable "Upper Limit": 0.026 mg/kg/day (NRC, 2000).
- Uncertainty Factor: 1000
- NOAEL: 1.32 mg/kg/day.
- Principal Study: Domingo et al., 1985.
- Comments: The NOAEL is derived from a study in which rats were given 0, 5, 10 and 50 ppm sodium metavanadate, in drinking water for 3 months. Impaired kidney function was seen at 50 ppm, and 10 ppm was considered a NOAEL. The Uncertainty Factor of 100 is the product of a 10-fold uncertainty in extrapolating from laboratory animals to humans, a 10-fold uncertainty to extrapolate from a subchronic to chronic exposure, and a 10-fold uncertainty to protect sensitive individuals.

The PPRTV 'subchronic' RfD is 0.0007 mg/kg/day. The study used as the "point of departure" (POD) was that of Boscolo et al. (1994). This study is a poor choice as a POD for several reasons. First, Boscolo and coworkers failed to report drinking water (the vehicle for vanadium sulfate) intakes so the doses cannot be accurately reported from the study. This is important because some researchers believe the reason laboratory rodents become dehydrated in these studies is the bad taste of vanadium in the drinking water. Secondly, the most sensitive effect found by Boscolo et al. (1994) was *increased* blood pressure at 0.12 mg/kg-day which was the NOAEL endpoint chosen by the authors of PPRTV. In humans who have taken vanadium as a dietary supplement or medication, however, there is either no change in blood pressure or a *decrease* in blood pressure is observed. Changes in kidney biomarkers or urine parameters have also not been reported. It is therefore our opinion that the best current subchronic RfD for "vanadium and compounds" would be that estimated by ATSDR (based on human data, above). The ATSDR value is, however, based on an 'unbounded' (freestanding) NOAEL so it is important to know that humans may be able to ingest higher doses without any adverse effects.

The PPRTV 'chronic' RfD is 0.00007 mg/kg/day. This value was derived by simply dividing the Boscolo POD (above) by an uncertainty factor of 10 "for extrapolation to chronic exposure duration from a subchronic study". As mentioned above, that study is not by this reviewer as a viable POD from which to derive an applicable RfD. It is our opinion that the current chronic PPRTV RfD will severely overestimate risk if used in concert with *any* oral exposure concentration. As an example of how egregiously flawed the current "provisional" chronic RfD is, we compare it to a list of RfDs currently listed on IRIS for some selected metals in Table 1. Based on this ranking, the PPRTV for vanadium is *more toxic than any other trace metal* in the IRIS database (and, if this RfD is to be believed, is eight times more toxic than free *cyanide*).

Also note that the combined Uncertainty Factor (UF) of 3000 appears to be unprecedented, as all of the UFs for trace toxic metals range from 1 to 1000. Given the fact that vanadium is, more likely than not, an essential element in the human diet, this reviewer recommends a combined UF of no greater than 300 for deriving an RfD from an animal study and no greater than 30 for deriving an RfD from a human study.

Also recommended is that USEPA adopt the National Research Council's Tolerable Upper Intake Level[1] (UL) as a "safe" dose for the daily (nondietary) intake of vanadium. We are in agreement with the PPRTV document that the form of vanadium, though bioavailability may differ, does not make a difference once it enters the bloodstream. The NRC recommends a LOAEL of 7.7 mg/kg/day based on the work of Domingo et al. (1985). The endpoint of that study is based on mild dose dependent lesions in kidneys and spleen. The severity of kidney lesions justified a UF of 3 to extrapolate from the LOAEL to the NOAEL. A UF of 10 was selected to extrapolate from laboratory animals to humans because no human and little animal data were available to use in the dose-response assessment. Another UF of 10 was selected for intraspecies variability. These three UFs are multiplied to yield an overall UF of 300 to extrapolate from the LOAEL in animals to derive a UL in humans.

Other Factors Modifying Toxicity

All of the scientific literature on the chemical disposition of vanadium in the environment is clear on the fact that the bioavailability of vanadium, including the pure compounds discussed above, is generally less than 5%. Additionally, the solubility of vanadium in natural waters rarely exceeds 5 ug/L. Finally, vanadium binds very strongly to soils and sediments, particularly substrates that have elevated levels of naturally occurring organic carbon in the subsurface environment. This is all very important when considering the "actual" exposure concentration (dose) to vanadium from various media at a hazardous waste facility.

Conclusions

Both a review of the PPRTV document and a comprehensive review of the pharmacological and toxicological effects reveals that "vanadium and compounds":

- are, for the most part, fairly insoluble compounds that are poorly absorbed by the GI tract
- are generally accepted as an "essential trace element" in the diet of both humans and mammals and have been used as a pharmacological agent for the treatment of diabetes (at relatively high doses) for decades
- show no convincing evidence of acute, subchronic or chronic toxicity to humans when exposure is via the *oral route*
- exhibit low oral toxicity to laboratory animals, with marginal effects on all target organ systems tested (e.g. hematology, reproductive, cancer) in both short- or long-term exposure studies

Both the subchronic and chronic provisional RfD values developed by the PPRTV document *fall within the range of extremely toxic metals* (currently cited in IRIS database) that are classically defined as metabolic poisons (e.g. antimony, arsenic, cadmium, cyanide, mercury). Vanadium and compounds are clearly on the opposite end of the spectrum, indeed, being offered widely to the public as nutritional supplements and as a panacea for Type 2 diabetes mellitus. The existing PPRTV values also appear to misuse or over apply conservative safety factors, not tempering their analysis with the plethora of studies that only show moderate toxic effects to animals following exposures to relative high dose ranges.

This reviewer recommends a chronic RfD of 0.026 mg/kg/day based on the recommendation of a Tolerable Upper Limit developed by the NRC (2000) which is based on a study that observed mild dose dependent lesions in kidneys and spleen in rats. This RfD falls with the range of less toxic metals that

are also known to be essential minerals in the diet of humans and animals (e.g. chromium(III), manganese, molybdenum, selenium).

Finally, although the environmental disposition is not a consideration when developing an RfD, the MassDEP needs to keep in mind that the solubility of naturally occurring vanadium compounds is very low. Thus, bioavailability in soils, surface waters and sediment is also anticipated to be low. Naturally occurring forms of vanadium bind strongly to environmental matrices so the potential for an adverse effect following inadvertent ingestion is negligible.

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[1] Tolerable Upper Intake Level (UL): the highest average daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects may increase.

Table 1
Ranked Metal RfDs for Selected Metals and Comparison to PPRTV for Vanadium

Constituent of Concern (USEPA IRIS)	Effect	Experimental Dose (mg/kg/day)	Inter- and/or Intraspecies UF	Subchronic-to-Chronic UF	Database Deficiencies UF	LOAEL to NOAEL UF	Total Combined UFs	Oral RfD (mg/kg/day)	Reference
Chromium III Salts	NOAEL	1468	100	1	10	1	1000	1.5	IRIS, 2013.
Barium and Compounds	LOAEL	63	100	1	3	1	300	0.2	IRIS, 2013.
Manganese	NOAEL	0.14	1	1	1	1	1	0.14	IRIS, 2013.
Nickel (soluble salts)	NOAEL	5	100	1	3	1	300	0.017	IRIS, 2013.
Selenium and Compounds	NOAEL	0.015	3	1	1	1	3	0.005	IRIS, 2013.
Silver	LOAEL	0.014	3	1	1	1	3	0.005	IRIS, 2013.
Molybdenum	LOAEL	0.14	10	1	1	3	30	0.005	IRIS, 2013.
Chromium VI	NOAEL	2.5	100	3	1	3	900	0.003	IRIS, 2013.
Beryllium Compounds	LOAEL	0.46	100	1	3	1	300	0.002	IRIS, 2013.
Cadmium	NOAEL	0.01	10	1	1	1	10	0.001	IRIS, 2013.
Antimony	LOAEL	0.35	100	1	1	10	1000	0.0004	IRIS, 2013.
Mercuric Chloride	LOAEL	0.29	100	1	1	10	1000	0.0003	IRIS, 2013.
Arsenic	LOAEL	0.0008	1	1	1	3	3	0.0003	IRIS, 2013.
Vanadyl Sulfate (PPRTV)	NOAEL	0.22	100	10	3	1	3000	0.00007	Boscolo, 1994.
Vanadyl Sulfate (NRC)	LOAEL	7.7	100	1	1	3	300	0.026	Domingo, 1985.