MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Phosphorus (white or yellow) (CAS# 7723-14-0)

FROM: Keisha Williams, Air Quality Division, Toxics Unit

DATE: February 3, 2017

SUBJECT: Review of Initial Threshold Screening Level

The Initial Threshold Screening Levels (ITSL) for phosphorus is 20 µg/m^3 on a 24-hour averaging time (AT). An acute ITSL was established in 2001 based on the occupational exposure limit from the American Conference of Governmental Industrial Hygienists (ACGIH) (MDEQ, 2001), but is now being changed based on an updated review of the literature.

The following references or databases were searched to identify data to determine the screening level: United States Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), the Registry of Toxic Effects of Chemical Substances (RTECS), the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, MDEQ Library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online definition search, National Library of Medicine (NLM), Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Status Report, EPA Aggregated Computational Toxicology Resource (ACToR) Database, EPA TSCATS database, EPA Superfund Provisional Peer Reviewed Toxicity Values, EPA Acute Exposure Guideline Levels for Airborne Chemicals, EPA High Production Volume Database, United States Department of Labor Occupational Safety and Health Administration Permissible Exposure Limits, Spacecraft Maximum Allowable Concentrations, Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profiles, California Office of Environmental Health Hazard Assessments Reference Exposure Levels, Chemical Safety Program Protective Action Criteria, Texas Commission on Environmental Quality Effects Screening Levels, and European Chemicals Agency Registered Substances Dossiers.

The purpose of this review was to A) verify whether white phosphorus and yellow phosphorus are the same and should receive the same ITSL, and B) update the ITSL based on the most current literature and understanding of the toxicity associated with phosphorus inhalation exposure.

NOTE: As of 2003, the Chemical Abstract Service number (CAS#) was changed from 7723-14-0 to 12185-10-3 (ACGIH, 2001). However, the 7723-14-0 number is still used by several agencies to refer to white or yellow phosphorus. To help prevent confusion, the old CAS # will still be used, and a footnote will be provided in the screening level database for reference.

<u>Objective A. To determine if white phosphorus and yellow phosphorus are the same chemical.</u>
White phosphorus and yellow phosphorus are synonyms for the same chemical (Figure 1) and the terms are used interchangeably for the same chemical (ACGIH, 2001; ATSDR, 1997). Databases also used to verify this are listed in Table 1. It should be noted that this chemical is also referred to as elemental phosphorus.

Figure 1. Molecular Structure of White or Yellow Phosphorus

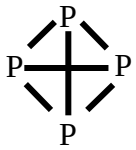

Table 1. Databases which confirm white phosphorus and yellow phosphorus are synonymous

Database Name-Webpage; all searched in August 2014
Integrated Risk Information System (IRIS)- http://www.epa.gov/iris/subst/0460.htm
National Institute for Occupational Safety and Health (NIOSH) Pocket Guide- http://www.cdc.gov/niosh/npg/npgd0507.html
Occupational Safety & Health Administration (OSHA) Index of Chemical Sampling Information- https://www.osha.gov/dts/chemicalsampling/data/CH_262600.html
Protective Action Criteria (PAC)- http://www.atlintl.com/doe/teels/teel/complete.asp Search CAS #12185-10-3
CAS Registry- http://www.cas.org/content/chemical-substances (Searched CAS #12185-10-3 and CAS#7723-14-0)

Objective B: To determine if the ITSL is to be changed based on the most current literature

Table 2 lists health benchmark values established by other agencies. No additional studies have been performed to determine if phosphorus is a possible carcinogen; as a result, it is still identified as a Class D chemical, not classifiable as to human carcinogenicity (EPA, 1993).

Table 2. Health Benchmarks for Phosphorus

Source	**Benchmark Value**
ACGIH (ACGIH, 2001)	Threshold Limit Value=0.1 mg/m^3 time-weighted average (TWA)
Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles (1997)	Acute Minimal risk level (MRL) = 0.02 mg/m^3, 24hr averaging time
Chemical Safety Program Protective Action Criteria (PAC) (Chemical Safety Program, 2012)	PAC-1=0.3 mg/m^3 PAC-2=0.51 mg/m^3 PAC-3=0.77 mg/m^3
IRIS (EPA, 1990)	Reference dose (RfD)=2.0 x 10^{-5} mg/kg/day
NIOSH (NIOSH, 2015)	Recommended Exposure Limit=0.1 mg/m^3 TWA
OSHA (OSHA, 2010)	Permissible Exposure Limit=0.1 mg/m^3 TWA
Texas Commission on Environmental Quality (TCEQ, 2014)	Short-term effects screening level (ESL) = 1 µg/m^3 Long-term ESL = 0.1 µg/m^3

The ATSDR's MRL was derived from a human study by White and Armstrong (1935). The original study could not be obtained, so the following is based on the ATSDR summary of the study. Male, human subjects were exposed for 5 minutes to 187 mg/m^3. Details about the subjects (age, etc) were not given. Concentrations as high as 514 mg/m^3 were also used with an exposure time of 15 minutes. Throat irritation, cough and headache were reported, and one man reported pain in his eyes and lungs. Besides the one individual, the study did not specify the number of subjects who experienced the listed adverse effects.

To derive the acute MRL, the lowest observable adverse effect level (LOAEL) was adjusted by ATSDR (1997) for time from a 5 minute to a 24-hour period, and uncertainty factors were used: 3 for LOAEL to no observable adverse effect level (NOAEL) extrapolation and 10 for intraspecies variation as shown in Equation 1. Justification for the temporal extrapolation from 5 minutes to 24 hours was described with: "Although a 5 minute exposure duration is usually too brief to consider for MRLs and expanding over a 24-hour period would result in an exposure level of 0.6 mg/m^3, further experiments indicated exposure for longer durations would result in more severe effects. In the field, white phosphorus smoke was generated at 0.1 mg/m^3 to protect soldiers from detection. In addition, the OSHA PEL is 0.1 mg/m^3. Therefore, expanding the 5 minute duration over 24 hours is reasonable" (ATSDR, 1997).

Equation 1.

$$MRL = LOAEL\ x\ minutes\ exposed \frac{1}{60\ minutes\ per\ hour}\ x \frac{1}{24\ hours}\ x \frac{1}{uncertainty\ factors}$$

$$MRL = 187\left(\frac{mg}{m^3}\right)\ x \frac{5\ minutes}{60\ minutes} x \frac{1}{24\ hours}\ x \frac{1}{3\ x\ 10}\ ,$$

where an uncertainty factor of 3 was applied for minimal LOAEL to NOAEL extrapolation and an uncertainty factor of 10 was applied for human variability.

MRL= 0.02 mg/m^3 x 10^3 µg/mg =20 µg/m^3, 24 hour averaging

The TLV, which served as the basis for the previously established acute ITSL, used a chronic inhalation study in rodents as the key study (ACGIH, 2001). The ATSDR MRL is based on acute inhalation effects in humans. As a result, the acute MRL is a more appropriate basis to use as the acute ITSL.

Based on a review of the current literature, the ITSL for phosphorus is 20 µg/m^3, 24-hour AT.

References

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MDEQ. 2012. *Memo from George Eurich to File for Phosphorous (yellow/white) (CAS# 7723-14-0). Subject: Screening Level Phosphorous (yellow/white) (CAS# 7723-14-0)*. July 25, 2012. AQD, MDEQ.

NIOSH. 2015. Phosphorus (yellow). Accessed July 31, 2015. The page was last reviewed on April 4, 2011 and last updated on February 13, 2015. http://www.cdc.gov/niosh/npg/npgd0507.html

OSHA. 2010. Phosphorus (yellow). Accessed July 31, 2015. https://www.osha.gov/dts/chemicalsampling/data/CH_262600.html

TCEQ. 2014. Effects Screening Levels (ESL) Lists Used in the Review of Air Permitting Data: Current ESL List. Accessed July 31, 2015. http://www.tceq.texas.gov/toxicology/esl/list_main.html/#esl_1

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

February 15, 2001

TO: File for phosphorus (yellow) (7723-14-0)

FROM: Marco Bianchi, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The Initial Threshold Screening Level (ITSL) for phosphorus (yellow) is 1 $\mu g/m^3$ based on an 8 hour averaging time. The following references or databases were searched to identify data to determine the ITSL/IRSL: IRIS-online, HEAST, NTP Management Status Report-online, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC-online, NIOSH Pocket Guide, and ACGIH Guide.

Phosphorus is a white to translucent yellow, soft, waxy, crystalline solid that darkens on exposure to light. It is used in gas analysis and in the manufacture of fireworks, explosives, incendiaries, smoke bombs, fertilizers, and other chemicals. Pastes of phosphorus were formerly used in rodent and cockroach control. Other allotropes of yellow (or white) phosphorus that share the same CAS number are red and black phosphorus. Black phosphorus has no present use, but yellow phosphorus (P_4), which appears to be the more common allotrope, is used to derive red phosphorus (P). Red phosphorus is a violet-red amorphous powder that has similar uses as yellow phosphorus, but its toxicity is much different and will not be part of this chemical evaluation. Due to a paucity of toxicity data, the American Council of Governmental Hygienist (ACGIH) Documentation of Threshold Limit Values and Biological Exposure Indices was the sole source of information to derive an ITSL for yellow phosphorus.

Phosphorus can be absorbed from the respiratory and gastrointestinal tracts. Experimental investigations in rats show the highest retention in the liver, skeletal muscle, gastrointestinal tract, blood, and kidney 5 days after oral administration. In the body, phosphorus is converted to phosphates. Urinary excretion, the chief mode of elimination, is largely as organic and inorganic phosphates. Following an oral dose, peak concentrations in liver are achieved within 2 to 3 hours. Inhalation of ^{32}P by animals showed a distribution pattern of lungs>bone>Iiver>kidney. The concentrations in soft tissues dropped rapidly when exposure ceased, but clearance from bone was slow. Skin and hair also contained a considerable amount of ^{32}P. Results were comparable when ^{32}P was administered by ingestion. Phosphorus can cause severe burns to the skin. Studies in rabbits found that sufficient quantities are absorbed from the burn area so as to cause abnormalities in the electrocardiogram and produce immediate and profound phosphorus/calcium electrolyte disruption.

According to the ACGIH, inhalation of more than 20 ppm phosphorus vapors by rats for 7 hours/day, 5 days/week (duration unknown) resulted in severe respiratory irritation and in a high mortality rate primarily due to pulmonary edema and bronchopneumonia. The observation of hyaline membrane formation suggested that the mechanism of action was similar to that of inhaled mineral acids. Other exposures from subcutaneous injections or parenteral administration of 0.05 mg/kg and 0.8 mg/kg, respectively caused bone changes and increased mortality.

In human studies, there have been numerous instances of acute yellow phosphorus intoxication following accidental ingestion. Three phases of the clinical course have been established: gastroenteritis, followed by some 48 hours of a relatively quiescent period, then death due to hepatic insufficiency and cardiovascular collapse. Signs and symptoms of acute phosphorus poisoning include nausea, vomiting, bloody diarrhea, jaundice, pruritis, and abdominal tenderness in areas of hepatomegaly. Hypoglycemia and acute hepatic necrosis leading to portal cirrhosis are serious life-threatening consequences. Cardiovascular collapse has been attributed to the metabolic derangement and a direct influence of phosphorus on the myocardium and blood vessels. The most common pathological finding at autopsy has been fatty degeneration of the liver and kidneys. Lymphocytosis and polycythemia have been associated with phosphorus intoxication. Other adverse effects due to phosphorus exposure are "phossy jaw" or necrosis of the jawbone, chemical burns from dermal contact, and sudden death after topical contact.

The ACGIH recommends a Threshold Limit Value (TLV) for yellow phosphorus of 0.1 mg/m^3 to minimize the potential for acute poisoning, but the margin of safety is unknown for the prevention of adverse effects from chronic exposures. As part of the ITSL derivation, a 100-fold uncertainty factor is applied to the TLV to account for any uncertainties in the data (Rule 232(1)(c)). This uncertainty factor should provide a margin of safety to adequately protect against chronic adverse effects to sensitive individuals in the general population.

The ITSL was determined as follows:

$$ACGIH\ TLV = 0.1\frac{mg}{m^3}$$

$$0.1\frac{mg}{m^3} \div 100 = 0.001\frac{mg}{m^3}$$

$$0.001\frac{mg}{m^3}\ x\frac{1000\frac{\mu g}{m^3}}{1\frac{mg}{m^3}} = 1\frac{\mu g}{m^3}$$

The ITSL for phosphorus (yellow) = 1 µg/m^3 based on an 8 hour averaging time

1. Documentation of Threshold Limit Values and Biological Exposure Indices. 1993 Phosphorus (yellow). American Conference of Governmental Industrial Hygienists (ACG1H), 6th Edition.

MB:DB
cc: Cathy Simon, AQD
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