

Charge Questions for the Revised Draft Risk Evaluation for C.I. Pigment Violet 29

Background

The *Draft Risk Evaluation for C.I. Pigment Violet 29* ([EPA-HQ-OPPT-2018-0604-0007](#)) (“draft risk evaluation”) was published on December 11, 2018. As per EPA’s final Risk Evaluation Rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726), the draft risk evaluation was subject to both public comments and peer review, which are distinct but related processes. EPA provided 60 days for public comment on all aspects of the draft risk evaluation, including the submission of any additional information that might be relevant to the science underlying the risk evaluation. This satisfied TSCA Section 6(b)(4)(H), which requires EPA to provide public notice and an opportunity for comment on a revised draft risk evaluation prior to publishing a final risk evaluation.

A Science Advisory Committee on Chemicals (SACC) peer review of the draft risk evaluation was held June 18-21, 2019, and a report of the peer review results was published in [September 2019](#). The Committee’s recommendations to EPA to improve the risk evaluation included:

- *“request an appropriate study to adequately determine bioavailability or bolster the evidence for poor water and octanol solubility in a well-laid out manner to support the Agency’s conclusions”*
- *“to improve the risk evaluation with respect to hazard to workers via inhalation to obtain and incorporate into the Evaluation better data and documentation from the manufacturer on conditions of use, exposures, and potential for worker exposures (e.g., collected using standard measurement techniques with adequate temporal and spatial coverage).”*

In response to the data needs identified by the SACC, EPA sought additional data to better understand the solubility and occupational exposures of C.I. Pigment Violet 29. Manufacturing stakeholders submitted some information to EPA voluntarily in response to EPA requests for clarification following the SACC review. EPA compiled the information received through correspondence with manufacturing stakeholders as a supplemental file to the revised draft risk evaluation entitled *Supplemental File: Information Received from Manufacturing Stakeholders* ([U.S. EPA, 2020a](#)).

Where the manufacturer information was insufficient to clarify the critical uncertainties, EPA used its test order authority under TSCA Section 4(a)(2) and Section 6(b). EPA required the generation and submission of solubility testing of C.I. Pigment Violet 29 in water and octanol, as well as a dust monitoring study of C.I. Pigment Violet 29 in the Sun Chemical manufacturing workplace conducted according to the [NIOSH 0600 Guideline](#) for respirable particles.

EPA used the information received in response to the TSCA test orders ([EPA-HQ-OPPT-2020-0070](#)) and through voluntary submissions by the manufacturer to revise the draft risk evaluation for C.I. Pigment Violet 29. These revisions include:

- Substantiation of the poor solubility of C.I. Pigment Violet 29 in water and octanol,
- Use of data on measured concentrations in the breathing zone of occupational workers to calculate risks, and
- Use of a surrogate chemical (carbon black) for evaluating human health risks based on data submitted by the manufacturer on the particle size distribution of C.I. Pigment Violet 29. Use of this surrogate reflects the smaller particle size distribution (1000 times smaller) reported by Sun Chemical in two data sets, compared to the particle size used in the draft risk evaluation (based on data provided prior to peer review from BASF).

EPA is moving forward with posting a Revised Draft Risk Evaluation for C.I. Pigment Violet 29 (“draft final risk evaluation”) for further public comment and letter peer review. **The following sections describe the charge questions for the general public comment period and the focus of the letter peer review on the new and updated information used in this risk evaluation.**

Physical Chemical Properties

Prior to the publication of the draft risk evaluation, EPA received a full study report that contained characterization of the melting point, vapor pressure, density, particle size distribution and the partition coefficient in *n*-octanol (log Kow) for C.I. Pigment Violet 29 from BASF (See Section 1.1 and Table 1-2 of the revised draft risk evaluation. The values provided for the water solubility and the octanol solubility were considered unacceptable for use in the draft risk evaluation for the following reasons. In the study, the log Kow was not measured directly; instead, it was estimated based on the solubility of C.I. Pigment Violet 29 in water and octanol, respectively. Additionally, there was some uncertainty associated with the water solubility (0.011 mg/L) and the octanol solubility (<0.07 mg/L, the Limit of Detection) since the limit of detection for the *n*-octanol solubility was higher than the measured water solubility value. Also, due to the particle-like nature of the substance, the method of filtration completely removed undissolved material during the studies. For these reasons, the studies were rated as unacceptable under EPA’s systematic review for data quality. Data quality evaluation results for the physical and chemical property studies are published as a supplemental file to the revised draft risk evaluation.

Thus, EPA used its TSCA Section 4 Test Order authorities to require the generation and submission of new information to decrease uncertainty associated with water solubility and octanol solubility in this revised draft risk evaluation of C.I. Pigment Violet 29. The TSCA Section 4 Test Order results reported the measuring solubility of C.I. Pigment Violet 29 in water (OECD 105, flask method) and in *n*-octanol (ETAD method, 2005). The partition coefficient (Log Kow) could not be measured due to the extremely low solubility of C.I. Pigment Violet 29 in octanol and water; therefore, EPA concluded that log Kow is not informative to the revised draft risk evaluation for C.I. Pigment Violet 29.

- **Question #1.** Based on the available data, do you agree with the conclusion that C.I. Pigment Violet 29 has extremely low solubility in octanol and water? Do you also agree with EPA's determination that log K_{ow} is not a relevant property for this chemical? Please explain your answers and provide any other information that would inform EPA on the physical/chemical properties of C.I. Pigment Violet 29.

Human Health Exposure – Particle Size

Human health exposure and hazards from inhalation of particles are associated with both the particle size as well as the concentrations of the particles in the air. Smaller particles are associated with deposition deeper in the lungs, in the alveolar region, than larger particles. For the draft risk evaluation, EPA obtained particle size information from BASF as part of an available compilation of physical and chemical properties for C.I. Pigment Violet 29, which indicated a median particle size diameter of 46.9 µm. Following the publication of the draft risk evaluation, EPA received additional particle size distribution (PSD) data from Sun Chemical, the sole United States manufacturer, describing a median diameter of C.I. Pigment Violet 29 of 0.043 µm, or 1000 times smaller than the initially-reported particle size used in the draft risk evaluation. In response to EPA questions concerning the PSD data, Sun Chemical provided a second characterization of the PSD of C.I. Pigment Violet 29, the reported the median particle diameter of this data set is 10.4 µm. Due to the large range in the size of particle diameters reported in the three studies of C.I. Pigment Violet 29 (ranging from 43 nm to 46.9 µm), the risks from inhalation of C.I. Pigment Violet 29 dust were characterized using all reasonably available data to represent this range of potential particle diameters. For specific information on the PSD data reported for C.I. Pigment Violet 29 please refer to Table 1-2 and Section 1.1 of the revised draft risk evaluation.

Human Health Exposure -- Concentrations in Air

Following the publication of the draft risk evaluation, EPA received the results of a workplace air monitoring study from Sun Chemical on October 25, 2019 via email ("Sun Chemical 2019 Study"). The information was provided voluntarily by the manufacturer in response to EPA's request for information on workplace monitoring of dust concentrations in air following the SACC meeting ([Sun Chemical, 2020](#)) (available in [U.S. EPA, 2020c](#)). Sun Chemical collected measurements from employees' personal breathing zones (PBZ) and analyzed total dust using [NIOSH method 0500](#). Worker activities performed during the personal sampling included various types of handling of solids, such as charging big bags to the blenders and repackaging. Individual exposures of respirable dust for six workers in the Sun Chemical 2019 Study ranged from 0.22 to 1.2 mg/m³. This study did not specifically measure C.I. Pigment Violet 29-containing respirable dust. For further information on the Sun Chemical 2019 Study refer to Table 1-2 in Section 1.1 of the revised draft risk evaluation.

To address critical uncertainties regarding occupational exposure to workplace respirable dust from the manufacture of C.I. Pigment Violet 29, EPA issued a TSCA Section 4(a)(2) test order (signed on Feb 28, 2020) to compel the submission of an Industrial Hygiene (IH) breathing zone monitoring study conducted according to the NIOSH 0600 test guideline. This information was identified as a critical data gap following the SACC review and Sun Chemical's submission of

breathing zone data (“Sun Chemical Study 2019”) for total respirable dust but not specific measurements of C.I. Pigment Violet 29 in dust. In June 2020, EPA received the results of the test order ([EPA-HQ-OPPT-2020-0070-0007](#)). The results of this study (Test Order Study) are provided in Table 1-2 and Section 1.1 of the revised draft risk evaluation.

Based on the two available sets of breathing zone data for respirable dust from the Sun Chemical manufacturing plant (the Sun Chemical Study 2019 and the Test Order Study), EPA estimated “central tendency” and a “high-end” exposure concentration of C.I. Pigment Violet 29 in the breathing zone. The central tendency is based on the average of the breathing zone measurements from the June 2020 Test Order Study which specifically measured respirable particles of C.I. Pigment Violet 29. In cases where the sample results were reported less than the detection limit, EPA used half of the limit of detection in the calculation of the arithmetic mean which is consistent with EPA’s approach in other risk evaluations ([EPA, 1994](#)). All but one of the samples from the June 2020 Test Order Study were reported as below the limit of detection. EPA assumed the “high-end” exposure is equal to the highest individual measured dust concentrations in the breathing zone across both the Sun Chemical Study 2019 and the Test Order Study.

- **Question #2.** Does EPA’s approach to inhalation exposure estimates make appropriate use of the received test data? Have uncertainties associated with the inhalation exposure estimates been adequately addressed? Please provide a rationale to your answer.
- **Question #3.** Do you have any specific recommendations to improve EPA’s calculation of inhalation exposures for C.I. Pigment Violet 29 based on the two available sets of breathing zone data?
- **Question #4.** Please provide any additional suggestions or additional factors that EPA should consider in estimating central tendency and high-end exposures for C.I. Pigment Violet 29 in the manufacturing workplace air.

Human Health Hazard – Selection of a Surrogate

The revised draft risk evaluation uses a different surrogate for inhalation hazard compared to the peer reviewed draft risk evaluation. EPA searched for a more appropriate surrogate for C.I. Pigment Violet 29 based on the smaller (and more respirable) PSD data reported by Sun Chemical (up to 1000 times smaller) compared to the draft risk evaluation (which used barium sulfate as a surrogate). EPA selected carbon black (CASRN 1333-86-4) as a more appropriate surrogate for C.I. Pigment Violet 29 based on the following characteristics.

1. Both chemicals are used as pigments or inks and are characterized as planar conjugated organic ring structures comprised primarily of multiple carbon rings.
2. The particle size of carbon black is similar to C.I. Pigment Violet 29. The particle size distributions of carbon black compared to C.I. Pigment Violet 29 are discussed in Section 3.2.3 of the revised draft risk evaluation. Reported particle sizes of 0.014 µm for high-surface area carbon black and 0.070 µm for low-surface area carbon black bracket the range of particle sizes for C.I. Pigment Violet 29 provided by Sun Chemical (0.043 µm).

3. Both chemicals have similar physical and chemical properties, including insolubility and density. The density is 1.97 g/cm³ for carbon black compared to 1.69 g/cm³ for C.I. Pigment Violet 29 and both are insoluble.
4. Both chemicals are respirable, poorly soluble materials with limited absorption and metabolism and have the same concern for inhalation exposure for increased lung burden for various lung pathologies if the deposition rate exceeds the clearance rate.
5. Carbon black is a well-studied chemical.

EPA considered these properties to be critical characteristics of a surrogate for C.I. Pigment Violet 29 and determined that carbon black matched these properties better than other potential surrogates. The use of carbon black as the surrogate is described in Section 3.2.3 of the revised draft risk evaluation.

To assess the appropriateness of carbon black as surrogate, the Multiple-Path Particle Dosimetry (MPPD) model was used to compare the predicted alveolar retention of C. I. Pigment Violet 29 following 13 weeks of exposure with the measured particle retention reported for carbon black. The MPPD models suggest that the increased lung burden can proceed into the lung overload situation at higher exposure levels and/or smaller particle sizes. This modeling analysis and its results support the use of carbon black as a surrogate for C.I. Pigment Violet 29 (see Appendix F of revised draft risk evaluation)

Selection of a surrogate chemical to inform the potential hazard of the target chemical is inherently a critical aspect of this assessment. Please carefully consider and robustly document your expert opinion concerning the selection of carbon black as the surrogate for C.I. Pigment Violet 29.

- **Question #5.** Is EPA's determination that carbon black matches the critical properties of C.I. Pigment Violet 29 and is an appropriate surrogate reasonable? If not, please provide suggestions of surrogates that may be better as a surrogate for C.I. Pigment Violet 29, along with additional justification for why the alternative surrogate is better than carbon black.
- **Question #6.** Are there other critical characteristics that should be considered in the selection of a surrogate? If so, provide detailed additional substantive information that EPA should consider.

Human Health Risk Characterization

To characterize human health risk, EPA calculated margins of exposure (MOEs) to workers from manufacturing and processing associated with chronic inhalation exposure to C.I. Pigment Violet 29. Inhalation was the only relevant route of exposure to workers as described in the human exposure assessment (Section 2.3 of the revised draft risk evaluation).

EPA calculated risk MOEs assuming three different particle sizes (0.043, 10.4, and 46.9 µm). These particle sizes represent the median values of the three sets of PSD data provided by BASF and Sun Chemical for C.I. Pigment Violet 29. Dust particles less than 100 µm are considered

non-respirable, and smaller particles are understood to have a higher deposition of the particles in the alveolar region of the lung. The PSD data are discussed in the previous section on Human Health Exposures – Particle Size Data. The PSD data are independent from the breathing zone data from the Sun Chemical 2019 study and the Test Order data.

A matrix of MOEs were calculated using the three assumed particle sizes for both “central tendency” and “high-end” exposures of C.I. Pigment Violet 29 in the breathing zone at the Sun Chemical manufacturing facility for occupational users (OUs) and occupational non-users (ONUs). These exposures are described previously in the section on Human Health Exposure – Concentrations in Air. Please refer to Section 4.2 of the revised draft risk evaluation and Table 4-3. For conditions of use downstream from the original single manufacturing facility for OUs and ONUs, the inhalation exposures of C.I. Pigment Violet are assumed to be no higher (equal) to that measured in the original Sun Chemical manufacturing facility.

- **Question 7.** Please provide any additional recommendations that EPA should consider for estimation of risk for conditions of use downstream from the original manufacturing site. What alternative assumptions could EPA make considering the lack of specific measurements of C.I. Pigment Violet 29 in air in downstream processing facilities?
- **Question 8.** EPA combined data for particle size from data sets that are independent of the data sets for concentrations measured in the breathing zone. Considering this, EPA calculated risks using the range of reported median particle sizes from small (0.043 μm), medium (10.4 μm) and large (46.9 μm) for both central tendency and high-end exposures. Is this matrix appropriate for estimation of the range of risks for OUs and ONUs? If not, please provide specific recommendations concerning alternatives that would provide less uncertainty in the risk characterization.