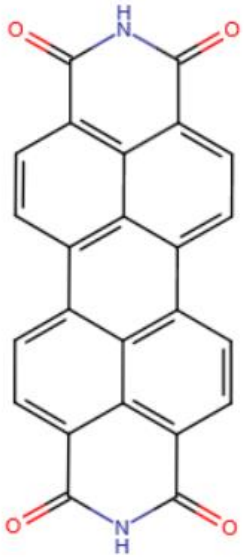
United States
Environmental Protection Agency

Office of Chemical Safety and
Pollution Prevention

Summary of External Peer Review and Public Comments and Disposition for C.I. Pigment Violet 29 (PV29) (Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone)

Response to Support the Revised Draft Risk Evaluation of C.I. Pigment Violet 29

CASRN: 81-33-4



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Introduction

EPA published the Draft Risk Evaluation for C.I. Pigment Violet 29 (PV29) on November 15, 2018 and accepted public comments until January 14, 2019. EPA accepted additional public comments from April 17, 2019 until May 17, 2019 following the release of 24 studies used in the draft risk evaluation of C.I. Pigment Violet 29, as well as the updated systematic review documents. EPA accepted a third round of public comments from June 10 to July 10, 2019 due to the publication of the PV29 Inhalation Risk Characterization Summary and the Updated Charge Questions for the peer review meeting of EPA's Science Advisory Committee on Chemicals (SACC) on the draft risk evaluation on June 18 to 21, 2019.

Materials on the draft risk evaluation are available at www.regulations.gov in docket EPA-HQ-OPPT-2019-0437.

This document summarizes the external peer review and public comments that EPA's Office of Pollution Prevention and Toxics (OPPT) received for the risk evaluation of C.I. Pigment Violet 29 (PV29). It also provides EPA/OPPT's response to the comments received from the peer review panel and the public.

EPA/OPPT appreciates the valuable input provided by the peer review panel and the public. The input resulted in numerous revisions to the hazard summary.

Peer review charge questions[1] are used to categorize the peer review and public comments into specific issues related to ten main themes.

1. Overall Content, Organization, and Presentation of the Document
2. Systematic Review Approaches and Clarity
3. Physical Chemical Properties and Environmental Fate
4. Exposure and Releases
5. Environmental Effects
6. Human Health
7. Risk Characterization and Risk Determination
8. Supplemental Analysis
9. Peer Review Comments on Confidential Business Information (CBI) Material
10. Other Peer Review Comments

All peer review comments for the nine charge questions are presented first, organized by charge question in the following section. These are followed by the public comments.

[1] These are the questions that EPA/OPPT submitted to the panel to guide the peer review process.

List of Comments Submissions

#	Docket File	Submitter
8	EPA-HQ-OPPT-2018-0604-0008	Stacy Tatman, Director, Environmental Affairs, Alliance of Automobile Manufacturers (Alliance)
9	EPA-HQ-OPPT-2018-0604-0009	Michelle Roos, Executive Director, Environmental Protection Network (EPN)
10	EPA-HQ-OPPT-2018-0604-0010	Georges C. Benjamin, Executive Director on behalf of American Public Health Association (APHA)
11	EPA-HQ-OPPT-2018-0604-0011	David Michaels, Epidemiologist, Professor, Environmental and Occupational Health, Milken Institute School of Public Health, George Washington University
12	EPA-HQ-OPPT-2018-0604-0012	Jonathan Kalmuss-Katz, Staff Attorney, Earthjustice and Randy Rabinowitz, Executive Director, Occupational Safety & Health Law Project
13	EPA-HQ-OPPT-2018-0604-0013	Richard A. Denison, PhD, Lead Senior Scientist, on behalf of Environmental Defense Fund (EDF)
14	EPA-HQ-OPPT-2018-0604-0014	Veena Singla, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al.
15	EPA-HQ-OPPT-2018-0604-0015	Brett Fox, International Union, United Automobile, Aerospace, and Agricultural Implement Workers of America (UAW)
16, 16(S)	EPA-HQ-OPPT-2018-0604-0016	Liz Hitchcock, Acting Director, Safer Chemicals Healthy Families et al.
17	EPA-HQ-OPPT-2018-0604-0017	Suzanne Hartigan, Senior Director, Regulatory and Technical Affairs, American Chemistry Council (ACC)
18	EPA-HQ-OPPT-2018-0604-0018	Rebecca L. Reindel, Senior Safety & Health Specialist, AFL-CIO
19	EPA-HQ-OPPT-2018-0604-0019	David Wawer, Executive Director, Color Pigments Manufacturers Association (CPMA)
20	EPA-HQ-OPPT-2018-0604-0020	Ansje Miiller, Director of Policy and Partnerships, Center for Environmental Health et al.
37	EPA-HQ-OPPT-2018-0604-0037	Jennifer Sass, Senior Scientist, Natural Resources Defense Council (NRDC)
43	EPA-HQ-OPPT-2018-0604-0043	Hanna Vesterinen, Research Consultant to UCSF PRHE et al.

#	Docket File	Submitter
44	EPA-HQ-OPPT-2018-0604-0044	Jonathan Kalmuss-Katz, Staff Attorney, Earthjustice and Randy Rabinowitz, Executive Director, Occupational Safety & Health Law Project
45	EPA-HQ-OPPT-2018-0604-0045	David Wawer, Executive Director, Color Pigments Manufacturers Association, Inc. (CPMA)
46, 46(S)	EPA-HQ-OPPT-2018-0604-0046	Richard A. Denison, Environmental Defense Fund (EDF)
47	EPA-HQ-OPPT-2018-0604-0047	Suzanne Hartigan, Senior Director, Regulatory and Technical Affairs, American Chemistry Council (ACC)
48	EPA-HQ-OPPT-2018-0604-0048	Liz Hitchcock, Acting Director, Safer Chemicals Healthy Families (SCHF) et al.
49	EPA-HQ-OPPT-2018-0604-0049	Kathy Pope, Environmental Protection Network (EPN)
55	EPA-HQ-OPPT-2018-0604-0055	Liz Hitchcock, Safer Chemicals Healthy Families (SCHF) et al.
71	EPA-HQ-OPPT-2018-0604-0071	Richard A. Denison, Environmental Defense Fund (EDF)
72	EPA-HQ-OPPT-2018-0604-0072	Suzanne Hartigan and Christina Franz, Senior Directors of Regulatory & Technical Affairs, American Chemistry Council (ACC)
73	EPA-HQ-OPPT-2018-0604-0073	Suzanne Hartigan, Senior Director of Regulatory & Technical Affairs, American Chemistry Council (ACC)
74	EPA-HQ-OPPT-2018-0604-0074	David Michaels, Department of Environmental and Occupational Health, The George Washington University
75	EPA-HQ-OPPT-2018-0604-0075	Gary E. Timm, Environmental Protection Network (EPN)
76	EPA-HQ-OPPT-2018-0604-0076	Jennifer Sass, Natural Resources Defense Council (NRDC)
77	EPA-HQ-OPPT-2018-0604-0077	Georges C. Benjamin, Executive Director, American Public Health Association (APHA)
78	EPA-HQ-OPPT-2018-0604-0078	Jonathan Kalmuss-Katz, Staff Attorney, Earthjustice et al.
79	EPA-HQ-OPPT-2018-0604-0079	Suzanne Hartigan, Senior Director, Regulatory and Technical Affairs, American Chemistry Council (ACC)
80	EPA-HQ-OPPT-2018-0604-0080	Michelle Roos, Environmental Protection Network (EPN)
81	EPA-HQ-OPPT-2018-0604-0081	Swati Rayasam et al., Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and

#	Docket File	Submitter
		Reproductive Sciences, University of California, San Francisco (UCSF PRHE)
82	EPA-HQ-OPPT-2018-0604-0082	Natural Resources Defense Council (NRDC) and Safer Chemicals Healthy Families (SCHF)
SACC	N/A	Science Advisory Committee on Chemicals (SACC)

(S) = Supplemental documents were provided with the comment and included in the summary

Comment Summary

Overall Content, Organization, and Presentation of the Draft Risk Evaluation

Charge Question 1: Please comment on the overall content, organization, and presentation of the draft risk evaluation of PV29. Please provide suggestions for improving the clarity and transparency of the information presented in the documents.

#	Summary of Comments for Specific Issues Related to Charge Question 1	EPA/OPPT Response
Draft was sufficiently clear and transparent		
8, 17	PUBLIC COMMENTS: • EPA's draft risk evaluation for PV29 is transparent in areas where the evaluation diverged from the problem formulation document, and in most cases, provided reasoning for changes. (8_1, 17_5) (note to reviewers, these parentheticals are used for EPA internal comment tracking purposes and will be removed from the final Response to Comment Document). • EPA clearly indicates that the conditions of use have been modified slightly since the problem formulation phase of the assessment. (8_7)	These organizational comments are appreciated and will be considered in a revised template for the next round of chemicals to be evaluated under TSCA section 6.
Need to improve clarity, transparency, and organization of rationale and conclusions		
SACC, 8, 17	SACC COMMENTS: • Carefully review and revise the Evaluation to ensure a logical and coherent flow to the discussion, and, to ensure that justifications are near their associated conclusions. The Committee noted that throughout the document, conclusions are stated without referencing the appropriate source or analysis that supports it. Sometimes these conclusions occur due to how the Evaluation is organized, forcing the reader to search a later part of the document or an entirely different document for the justification of the conclusion. An example of this occurs in Section 2.4.2 Conceptual Models (page 14) that assumes that	EPA has updated the risk determination format for increased clarity regarding the unreasonable risk determination and the risk considerations for each condition of use. These organizational comments are appreciated and will be considered in a revised template for the next round of chemicals to be evaluated under TSCA section 6. While EPA believes that discussions of the rationale for the determination of unreasonable risk is outside the scope of the SACC, EPA is committed to providing the public with sufficient information on the basis for that determination. TSCA requires EPA to determine whether chemicals in the marketplace present unreasonable risks to health or the

	PV29 has low hazard and limited exposures (a conclusion) to justify the model before hazard (Section 3) and exposure (Section 4) have been discussed. • Clearly state preliminary suppositions in the final risk determination and ensure that the hazard statement contains associated limitations and uncertainties. The Committee noted that there is information reported in EPA's Problem Formulation document that is referenced in the risk assessment. This information represents preliminary suppositions not discussed in a definitive manner in the Evaluation. Of most concern to the Committee were the preliminary suppositions that impacted Human Exposures (Section 3.3). The Committee concluded that broad statements such as "low hazard was reported for all routes of exposure in human health testing" did not adequately portray the associated uncertainty due to limited data and endpoints considered. The hazard statement at a minimum should identify the animal models and endpoints used. • Define unreasonable risk under the TSCA legislative requirement and describe in general how the threshold between reasonable and unreasonable risk is determined. • Consider using the slide presentation given by EPA on Thursday as a guide for organizing the draft risk assessment document. <u>PUBLIC COMMENTS:</u> • At present, OPPT does not sufficiently describe its rationale for the conclusion of "no unreasonable risk" for PV29. While we support this determination, we have concerns about how this method will be applied to future chemical risk	environment. While the law does not specifically define this term, during the risk evaluation process EPA weighs a variety of factors including the effects of the chemical on human health or the environment, who are exposed (including any sensitive subpopulations), the severity of the hazard, and uncertainties. This approach is outlined in EPA's 2017 *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* rule ("Risk Evaluation Rule") preamble on how risk evaluations will be conducted. [82 FR 33726, at 33735 (July 20, 2017)] Each draft risk evaluation details those factors and describes for the public which conditions of use were preliminarily identified to have unreasonable risk for a chemical. For PV29, these factors included workplace exposures based on monitoring information from the sole U.S. manufacturer, Sun Chemical. When appropriate, in the risk evaluation, EPA will consider exposure scenarios both with and without engineering controls and personal protective equipment (PPE) that may be applicable to particular worker tasks on a case-specific basis for a given chemical. These assumptions are described in the uncertainties sections that were added throughout the final Risk Evaluation to more adequately discuss uncertainties and their effect on the unreasonable risk determination for each condition of use in Section 5.2. TSCA requires EPA to use reasonably available information and best available science in its risk evaluation. Utilizing the systematic review process, EPA used reasonably available data and best available science in a weight of the scientific evidence analysis. EPA identified uncertainties regarding the information that is reasonably available to characterize PV29's solubility and occupational worker inhalation exposure in Section 2.3.4 of the final Risk Evaluation. These uncertainties resulted in EPA requiring testing of PV29 to develop and submit new information in order for EPA to increase certainty in the final Risk Evaluation of PV29 under TSCA section 6(b). Test data has been reviewed for data quality according to the relevant

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	evaluations. We request that OPPT expand the narrative in the risk evaluation document to more clearly describe how the available information supports its findings. (8_6) • EPA should consider making clear how it determined the existing data set was sufficient to develop a risk characterization and determination. (17_1)	data quality evaluation metrics and incorporated into the final Risk Evaluation.
Need to improve clarity and transparency of study quality evaluations		

17, 46	PUBLIC COMMENTS: • More detail in the risk evaluation regarding how EPA evaluated study quality would improve transparency. (17_14) • EPA should always make study reviewer comments public in order for the public to understand the rationale behind its study quality scoring decisions and to have a transparent record of when and why changes to scores are made. (46_11)	Along with publishing the problem formulation for PV29, EPA published the inclusion/exclusion criteria statements used during full text screening for each chemical in appendices to those documents as well as a separate document titled *Application of Systematic Review in TSCA Risk Evaluations* that described the data quality criteria used for each discipline and outlined data integration strategies which are being used for the risk evaluations. EPA initially released the SR Supplemental File without the EPA reviewer's comments due to concerns that the comments might contain information claimed CBI. The Updated SR Supplemental File, released on April 4, 2019, made publicly available the EPA reviewer's comments related to the data quality evaluation of the physical chemical characteristics, environmental fate, environmental hazard and human health studies (EPA-HQ-OPPT-2018-0604-0040). EPA is making reviewer comments public with the release of the Systematic Review Companion documents for the final Risk Evaluation to increase transparency. In addition, an ad hoc committee of the National Academies of Sciences, Engineering, and Medicine is reviewing EPA's guidance document on *Application of Systematic Review in TSCA* [Toxic Substances and Control Act] Risk Evaluations (EPA 2018) and associated materials developed subsequent to its issuance. The committee is considering public comments on the document, EPA's responses to public comments, and enhancements to the systematic review process reflected in documentation of the first 10 chemical risk evaluations. The committee will determine whether EPA's process is comprehensive, workable, objective, and transparent. Recommendations for enhancements to EPA's 2018 guidance document will be made. More information and details about the NAS review effort are available here: https://www.nationalacademies.org/our-work/review-of-epas-tsca-systematic-review-guidance-document

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Include measures and discussion of uncertainty and variability with numerical values		
SACC, 46	SACC COMMENTS: • Include measures and discussion of uncertainty and variability with all numerical values. The SACC Committee noted that in the Evaluation, numerical values are presented without associated statements of confidence or measures of variability, especially the physical-chemical values. The Committee noted that risk assessments typically include discussions of uncertainty and variability with reported values. The scientifically reasoned basis for inclusion, exclusion or selection of data values is also expected. For example, is the indirect photodegradation half-life of 7 hours listed in Table 3-1 consistent with overall conclusions that the chemical is very persistent? Estimates of water solubility of PV29 are also inconsistent. PUBLIC COMMENTS: • Major data gaps have not been acknowledged or addressed by EPA. EPA needs to forthrightly address the data gaps and uncertainties including those flagged by EU authorities. (46_27)	EPA has made an effort to increase the discussion of uncertainty surrounding the numerical values used in the assessment in Section 4 of the final Risk Evaluation. Where applicable, the use of a particular value over another is explained and justified with a discussion of uncertainties. EPA identified uncertainties regarding what information was reasonably available to characterize PV29's solubility and occupational worker inhalation exposure in Section 2.3.4, as well as EPA responses to the submitted information from the Section 4 Test Order in the Test Order docket (EPA-HQ-OPPT-2020-0070-0008). These uncertainties resulted in EPA requiring testing of PV29 to develop new information in order for EPA to increase certainty in the final Risk Evaluation of PV29 under TSCA section 6(b). Test data has been reviewed for data quality according to the relevant data quality evaluation metrics and incorporated into the final Risk Evaluation so that uncertainty is reduced.
Need to improve transparency of risk evaluation process and procedures		
SACC, 8, 13, 17, 49	SACC COMMENTS: • Include a short history or basis on why PV29 was originally selected for inclusion on EPA's Work Plan and discuss how those concerns have been addressed in the assessment. The Committee felt that this section is important in establishing the justification for the risk evaluation and provides	In the Introduction (Section 1) of the final Risk Evaluation EPA incorporated a narrative explaining the basis for the inclusion of PV29 on the TSCA Work Plan, which was developed as a screening tool prior to full risk assessment. The final Risk Evaluation also describes the current understanding of the

	context and importance for the final risk determination. PUBLIC COMMENTS: • Guidance documents that detail the internal processes and procedures for risk evaluation under TSCA should be generated and made publicly available. (17_27) • EPA's description of its approach to data integration in its draft risk evaluation for PV29 is severely lacking. (13_231) • EPA should provide more detail on the tiered approach used in this risk evaluation. This should include developing guidance detailing its tiered assessments process, especially on how EPA will conduct higher-tier assessments triggered by lower-tier outcomes. (17_10, 17_28) • Recommend that EPA provide additional information regarding why a quantitative screening-level exposure assessment was added. (8_8, 17_6) • EPA should clarify why PV29 was poorly characterized for the Work Plan, and how the lessons from that characterization might inform EPA's prioritization process for the TSCA Active Inventory. (17_22) • The lack of transparency in this risk evaluation will create a precedent of making "no unreasonable risk" determinations based on proprietary information. (49_1)	chemical's risks as a result of the full TSCA risk evaluation process. EPA has finalized and made publicly available a document *Application of Systematic Review in TSCA Risk Evaluations* to provide the public with continued transparency regarding how EPA plans to evaluate scientific information. This document outlines EPA's initial work on systematic review. This document can be accessed at: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/application-systematic-review-tsca-risk-evaluations In addition, EPA anticipates feedback from the National Academy of Sciences (NAS) on its systematic review process and will carefully review and implement relevant NAS recommendations as appropriate. EPA has incorporated references to this process in the final Risk Evaluation document in Section 1.6 of the final Risk Evaluation EPA continues to improve upon its data integration strategies, which are expected to be more formal and structured for the next set of TSCA chemical risk evaluations. The anticipated feedback from the NAS on EPA's systematic review process will inform this. EPA is not implementing a fixed approach concerning tiered risk evaluations as suggested by the commenter. As evidenced by the Risk Evaluations for each of the first 10 chemicals evaluated under TSCA, EPA is adopting a fit-for-purpose approach which makes the determination based on the reasonably available data characterizing the conditions of use, hazards and exposures. The decision to adopt a screening-level approach for the Risk Evaluation of PV29 was made as a result of reasonably available information indicating hazards for all routes of exposure except for inhalation are low, and exposures through all routes except manufacturing, processing and industrial/commercial uses are expected to be limited.

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		With regard to the comment pertaining to proprietary information, the Agency has made a final determination on the CBI claims made for PV29 and this can be accessed at FOIAonline at: https://foiaonline.gov/foiaonline/action/public/submissionDetails?trackingNumber=EPA-HQ-2019-001853&type=request In all instances, non-CBI versions of the study reports were made available to the Agency and can now be accessed in the public docket.
Report would be improved by adding graphics, figures, and/or tables		
SACC	SACC COMMENTS: • Develop a flowchart/decision tree to more adequately describe the risk evaluation. The Committee concluded that uncertainty in decisions could be more transparently communicated and evaluated using appropriate graphics. The Committee discussed decision tree diagrams as well as logic model diagrams. Such diagrams could be adapted to display associated confidence at each decision point in order to clarify overall confidence in the conclusion (see also discussion in Question 2). • Describe in more and better detail the systematic review process (Section 2.5) and its results. The results of systematic review are discussed in prose where one or two diagrams would significantly improve the clarity and transparency of the process. Graphical and/or tabular summaries are needed of the number of abstracts, reports and manuscripts reviewed, and reports and manuscripts accepted and rejected and at what stage in the review process.	In response to these comments, EPA has integrated flow-charts outlining the various steps of the literature search and the number of references that were identified at each step of the literature search and screening processes in Section 2.5.1. These literature flow diagrams have also been incorporated into the other evaluations for the first 10 chemicals evaluated under TSCA. For additional information about how the literature search strategy for PV29 was conducted, please consult the document entitled, "*Strategy for conducting literature searches for Pigment Violet 29 (PV29): Supplemental document to the TSCA scope document*," available at: https://www.epa.gov/sites/production/files/2017-06/documents/pv29_lit_search_strategy_053017_0.pdf

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Need to improve transparency of external review processes		
16(S), 17, 82	PUBLIC COMMENTS: • Coordination with other federal agencies and other EPA program offices should be clearly described. (17_11) • The final Risk Evaluation should include all peer reviewer comments and how EPA responded to them. (16(S)_23) • EPA did not provide any means for the public to know about and have confidence in the extent of EPA CBI reviews, the determinations being reached, and the provision of access to information the law requires be provided. (82_6)	EPA's discussions and consultation with NIOSH are reflected in the updated screening-level assessment of risks from inhalation exposure in Section 4.4 of the final Risk Evaluation. EPA does not share internal deliberative comments from the interagency review process. All EPA responses to SACC recommendations are provided in this Response to Comment document. A final report of the proceedings of the TSCA Scientific Advisory Committee on Chemicals (SACC) meeting held on June 18-21, 2019 has been made publicly available in the docket (EPA-HQ-OPPT-2018-0604). As explained in a March 21, 2019 transmittal memorandum available in the docket, the Agency made a final determination on the CBI claims of the studies used in this assessment which can be accessed at FOIAonline at: https://foiaonline.gov/foiaonline/action/public/submissionDetails ?trackingNumber=EPA-HQ-2019-001853&type=request. In all instances, non-CBI versions of the study reports were made available to the Agency and were added to the public docket.
Need to improve access to information sources		
SACC, 13, 17	SACC COMMENTS: • Provide cross references to relevant documents and associated information. The Committee understood that in order to keep the Evaluation relatively short and concise, EPA chose to not repeat information available in other documents or information sources, primarily other EPA documents that provide relevant guidelines. To assist the reader, the risk evaluation document	EPA has made every effort to update the final Risk Evaluation to provide links to accommodate easier access to all publicly available information, data and guidance referenced in the risk evaluation. This includes Safety Data Sheets, information received from manufacturing stakeholders of C.I. Pigment Violet 29 and the full study reports used in the evaluation. All of these materials have been made publicly available in the docket for C.I. Pigment Violet 29 (EPA-HQ-OPPT-2018-0604)

	should provide easy reference, and, where possible, internet links to these key documents or information sources. For example, reviewing the section on "environmental release and exposure," a reader should be able to click on a link to relevant EPA guidance documents on this topic. The SACC noted that recent TSCA legislation established that public review of (including access to) supporting data is part of the process ensuring transparency in the evaluation of health risk from large quantity manufactured chemicals in the US. All documentation and studies used for the assessment, especially health and safety information, should be made available to the public. Access to certified CBI is still problematic. PUBLIC COMMENTS: • EPA needs to link directly to the Safety Data Sheets (SDSs) used in reviewing engineering controls and PPE, or directly provide them. (13_172) • EPA should provide access to the SDS and industry statements on which it relies to discount potentially relevant routes of exposure. (13_172) • Sun Chemical's SDS is not available to the public; without this SDS, it is not possible to assess the accuracy of EPA's claims regarding engineering controls and PPE. (13_173) • Most information obtained from industry should have been made public, particularly the approximate maximum workplace air concentration and daily discharge rate from Sun Chemical. (13_34) • EPA must immediately make public the details of the Mott 2017 personal communication, and all other personal communications relevant to the risk evaluation. (13_170, 15_9)	in a supplement entitled, *Supplemental File: Information Received from Manufacturing Stakeholders* U.S. EPA (2020a). EPA has included copies of the Safety Data Sheets (SDSs) as well as information received via correspondence with manufacturing stakeholders that contain data used to characterize occupational and environmental exposures to PV29 (including the Mott 2017 personal communication). These data are available in a supplemental file in the docket for the final Risk Evaluation entitled, "*Supplemental File: Information Received from Manufacturing Stakeholders*." U.S. EPA (2020a) EPA has worked with the data owners of the studies summarized in the ECHA database and has included fully unredacted or partially redacted versions of these studies in the public docket for PV29 (EPA-HQ-OPPT-2018-0604). A summary of the redaction status of each study report can be found at https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0604-0021. The inclusion of the full study reports increases the transparency of the Risk Evaluation process as it relates to PV29.

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	• The exposure sampling data and detailed information should be available for public review so that commenters can provide their own interpretations to the docket. The public should not have to rely on the judgment of the manufacturer and the Agency that this is indeed the maximum exposure level. (15_10, 15_15) • EPA should consider more clearly linking the robust study summaries available on ECHA's website to the outcome of the risk evaluation, to enhance clarity in how the data were applied. (17_8)	
Need to improve transparency of occupational exposure data and PV29 uses		
SACC, 13, 15, 16, 17, 18	SACC COMMENTS: • Include more information on production volume and derivative products. The Committee discussed the need for better discussion of PV29 production volume in the report. Missing was a discussion of how the quantity of PV29 produced makes this a high production volume chemical, or how the quantity produced relates to production volumes of other priority chemicals or high production chemicals. The Evaluation reports that 90% of PV29 production is used to make another pigment. This, combined with the observation that the European Union (EU) is assessing risks of both pigments together, suggested that the assessment should discuss both pigments in a single assessment. Needed is the rationale for why EPA has chosen to assess PV29 alone. The Committee would have also liked a summary/comparison of the structure, toxicity	As indicated above, EPA has included a narrative explaining the inclusion of PV29 on the TSCA Work Plan. Included in this narrative is an explanation of how the total production volume of the chemical relates to the current understanding of the conditions of use. In particular, the vast majority of overall production volume is consumed at the manufacturing site as an intermediate for the production of other pigments. EPA also notes that production volume of this chemical, ~600,000 lbs. in 2015, falls well below the threshold for a high production volume chemical which EPA considers to be 1,000,000 lbs; therefore, a discussion of PV29 being a high production volume chemical is not warranted. The risks of another pigment produced using Pigment Violet 29 as an intermediate is outside the scope of this risk evaluation. This chemical, if identified to meet the criteria for assessment through the prioritization would be considered in its own risk evaluation. PV29 was included in the prioritization list without other perylene pigments because information specific to PV29 were identified during the prioritization process that indicated that it was potentially hazardous to aquatic organisms. As explained in Section 1 of the final Risk Evaluation, review of the data led EPA to

	concerns, and exposure profiles for both chemicals. PUBLIC COMMENTS: • EPA does not detail the efforts it made to research all reported PV29 uses and explain why uses it initially identified were dropped. (16_41) • EPA should provide information on how it determines what conditions of use are in/out of scope. (17_30) • This draft risk evaluation on PV29 is incomplete and not transparent about the information it relied on to assess health risk to working people. (18_16)	conclude that these aquatic toxicity data as well as other data used in the prioritization process are no longer applicable to C.I. Pigment Violet 29. Regarding the decision to assess PV29 alone, EPA incorporated a narrative explaining the basis for the inclusion of PV29 on the 2012 Work Plan in the Introduction (Section 1) of the final Risk Evaluation. A list of "other uses" was compiled during EPA's initial search for PV29 conditions of use. This list of other uses included the following: Applications in odor agents, cleaning/washing agents, surface treatment, absorbents and adsorbents, laboratory chemicals, light-harvesting materials, transistors, molecular switches, solar cells, optoelectronic devices, paper, architectural uses, polyester fibers, adhesion, motors, generators, vehicle components, sporting goods, appliances, agricultural equipment and oil and gas pipelines (EPA-HQ-OPPT-2016-0725-0004). However, no further evidence was found or submitted during the scope, problem formulation and draft risk evaluation steps to support these "other uses" as intended, known, or reasonably foreseen conditions of use for C.I. Pigment Violet 29. As a result, these uses were determined to not be intended, known, or reasonably foreseen conditions of use. As stated in C.I. Pigment Violet 29's Problem Formulation, to determine the current conditions of use of C.I. Pigment Violet 29 and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA's review of published literature and online databases including the most recent data available from EPA's Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of C.I. Pigment Violet 29 and queried government and commercial trade databases. EPA also received comments on the Scope of the Risk Evaluation for Pigment Violet 29 U.S. EPA (2017) that

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		were used to determine the current conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. TSCA Section 3(4) grants EPA the authority to determine what constitutes a condition of use for a particular chemical substance. In the case of PV29, as described in the preceding response, there were a group of "other uses" that were identified early in the process with poor quality references. Subsequent to the publication of the scope document, no further information was found or received by EPA that substantiated any of the uses with limited and poor-quality references that had been characterized as "other uses". As a result, these uses were determined to not be intended, known, or reasonably foreseen and are not conditions of use. Following the publication of the Draft Risk Evaluation, EPA communicated with the manufacturing stakeholders to clarify the uncertainties indicated by the commenters related to a lack of information characterizing the full range of job tasks, chronic health/exposure studies, workplace air monitoring data across shifts and tasks, assumptions about volumes handled by downstream processors/users, and PPE assumptions. The results of this information gathering have been compiled and released to the docket in a supplement entitled, *Supplemental File: Information Received from Manufacturing Stakeholders* U.S. EPA (2020a).
Need to improve clarity and transparency of study quality evaluations		

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17, 46, 47	PUBLIC COMMENTS: • More detail in the risk evaluation regarding how EPA evaluated study quality would improve transparency. (17_14, 47_2) • EPA should always make study reviewer comments public in order for the public to understand the rationale behind its study quality scoring decisions and to have a transparent record of when and why changes to scores are made. (46_11)	On April 4th, 2019, EPA released an updated version of the systematic review documents for the PV29 risk evaluation. The systematic review materials for PV29 were updated following the release of study reports to include the reviewer's comments and a reevaluation of several human health studies (EPA-HQ-OPPT-2018-0604-0040). These updated systematic review data quality evaluation results were also released as supplemental documents to the final Risk Evaluation. This enhances the transparency of the systematic review portion of the risk evaluation.
EPA did not use its legal authority under TSCA to collect data, and it should		
13, 16, 18, 44, 75	PUBLIC COMMENTS: • EPA did not use its full authority to collect the relevant toxicity and exposure data. (18_14) • EPA must consider "reasonably available" information, and thus EPA must use its authorities under TSCA 4 and 8 to obtain additional information, this includes relying on more than voluntary data submissions. EPA is still relying solely on "readily" available information, not all reasonably available information. Relying solely on voluntary requests for information, may result in limited, biased, inaccurate, or incomplete information on the chemicals. (13_268) • Rather than relying on voluntary requests for information which are often limited, biased, inaccurate, or incomplete (*e.g.*, submissions by Sun Chemical Corporation and Color Pigments Manufacturers Association), EPA should use its mandatory authorities to collect the relevant toxicity and exposure data, and reissue for public	Uncertainties were identified in the draft Risk Evaluation regarding reasonably available information characterizing PV29's solubility and occupational inhalation exposure. To address these uncertainties and respond to comments received, EPA used its Test Order authority under TSCA section 4(a)(2) to requiring testing of PV29 to develop new information to increase certainty in the final Risk Evaluation of PV29 under TSCA section 6(b). EPA required the following testing to be conducted for PV29: 1) Solubility of PV29 in water 2) Solubility of PV29 in octanol 3) A workplace dust monitoring study of particles not otherwise regulated, conducted according to the NIOSH 0600 guideline available Test data has been received and reviewed for data quality according to the relevant data quality evaluation metrics and incorporated into the final Risk Evaluation. More information about the Section 4 Test Order for PV29 can be found in the Section 4 Test Order docket (EPA-HQ-OPPT-2020-0070-0008).

#	Summary of Comments for Specific Issues Related to Charge Question 1	EPA/OPPT Response
	comment. (13_274, 13_284, 13_286, 18_16, 18_16, 44_4) • Necessary information includes conditions of use, exposures, workplace monitoring, environmental releases, hazards, potentially exposed or susceptible subpopulations, ecotoxicity. (13_80, 13_84, 13_89, 13_244, 13_284, 16_3, 16_104, 16-110, 75_2) [For specific data requests, see comment summary sections 4.5, 5.1, and 6.7.]	
Violation of TSCA by not releasing full studies due to CBI claims		
9, 11, 12, 13, 14, 16, 20, 44, 46, 46(S), 48, 49, 55, 75, 76, 82	PUBLIC COMMENTS: • Failure to release the 24 CBI studies violates section 14 of TSCA, reflects a troubling lack of transparency, and will frustrate the ability of interested parties to review and submit comments on the science EPA cites to support its risk evaluation and to participate meaningfully in the peer review process. (13_32, 20_1) (55_9) • TSCA restrictions on disclosure of CBI do not apply to health and safety studies that are submitted for chemical substances which have been offered for commercial distribution [TSCA section 14(b)(2)]. TSCA defines "health and safety study" broadly. EPA should immediately release all of the full study reports to the public under TSCA 14b. (9_8, 12_16, 12_36, 13_16-20, 13_11, 13_32, 14_5, 16_15-17, 20_1-9, 44_6, 46_5, 48_2, 49_3, 55_7-9, 76_2, 82_6) • Threats from industry cannot justify compromising the transparency that Congress required under TSCA section 14(b). (46(S)_6) • Withholding the full study reports violates requirements of public notice and	On March 21, 2019, EPA released copies of the 24 study reports claimed as CBI to the public docket. Fifteen study reports were completely released without redactions, while nine reports remain partially CBI with certain information redacted. Consistent with Agency regulations concerning the review of confidential business information claims located at 40 CFR Part 2, Subpart B, the Agency, in December 2018, requested substantiation of the CBI claims from the affected businesses. Subsequently these entities provided responses to the substantiation request. In fifteen instances, the CBI claims associated with the study reports were removed in full by the data owners. In nine instances, the CBI claims were reduced in scope. For the reasons explained in the final confidentiality determination, EPA concluded that TSCA section 14 did not govern these studies and determined that the information redacted in the nine studies at issue is entitled to confidential treatment. The Agency made a final determination on the CBI claims and this can be accessed at FOIAonline at: https://foiaonline.gov/foiaonline/action/public/submissionDetails ?trackingNumber=EPA-HQ-2019-001853&type=request. In all instances, these study reports were made available to the Agency and can now be accessed in the public docket. The study reports as well as a summary of the

	comment in section 6 of TSCA and hinders the peer review process. Providing summaries of study reports does not adequately meet these requirements. Only access to the full studies will allow a meaningful opportunity to comment whether the studies support EPA's claim that PV29 does not present unreasonable risk. (9_9, 11_2, 12_37, 13_26-27, 14_5, 16_19, 20_6, 46_5, 55_7, 82_6) • It is ironic that EPA believes it can base regulatory decisions on PV29 on data that are unavailable to the public while taking a diametrically opposite position in its recent proposed rule purportedly promoting "transparency" in regulatory science. *Federal Register* 18768 (April 30, 2018). (20_8) • The heavy data redactions from the reproductive/developmental toxicity screening study are so extensive as to preclude the ability of the public to have any confidence at all in EPA's many decisions in the draft risk evaluation that are based on it. (44_9, 46_2-3, 55_8, 75_6) • EPA's indication that it will allow members of the SACC to review the 24 studies but deny access to the public only compounds this lack of transparency. (13_25, 16_19, 20_7) • EPA has not described the claims of confidentiality that would justify withholding all or parts of the PV29 health and safety studies. Under TSCA, the only portion of a health and safety study that can be treated as CBI is information "that discloses processes used in the manufacture or processing of a chemical substance." The studies available for PV29 are unlikely to contain this type of information. (13_21, 16_18, 20_4)	redaction status of each study report can be found in the PV29 docket (EPA-HQ-OPPT-2018-0604-0021). As a result of the release of this information and input from the public about the application of the data quality evaluation process, EPA re-evaluated the studies and updated the data evaluation scoring sheets based on public comments. These updated systematic review scoring sheets also contain the reviewer comments which were previously not included because of concerns about the CBI status of the studies. The updated SR Supplemental File, available in the public docket for PV29 (EPA-HQ-OPPT-2018-0604), provides a more transparent approach than previously provided by including the metric scores, weighting, reviewer's comments and the study's overall score. The information provided in the public docket for PV29 enabled a meaningful opportunity to comment on the draft risk evaluation and was consistent with TSCA 26(j) and 40 CFR 702.51 provisions on public availability of information. EPA reviews confidentiality claims asserted for information that is reported to, or otherwise obtained by, EPA under TSCA in accordance with TSCA section 14(f) and (g). Confidentiality claims asserted for business information that is not subject to a specific statutory review requirement are reviewed in accordance with 40 CFR 2.204(a).

#	Summary of Comments for Specific Issues Related to Charge Question 1	EPA/OPPT Response
	• EPA should have reviewed all confidentiality claims asserted in at least approximately one-fourth of the information submissions it received. (13_33)	
Support for EPA's handling of CBI		
19, 45, 47, 72	PUBLIC COMMENTS: • EPA is correct to protect the CBI status of health and safety studies that are voluntarily submitted. The language in TSCA section 14 does not require EPA to publish confidential health and safety studies. (19_19-20) • EPA determined correctly that studies owned by foreign companies submitted voluntarily to EPA qualify for CBI protection under FOIA, and that analysis under TSCA is inapplicable. (47_4, 72_1) • However, EPA significantly overstates what is required of the Agency under TSCA section 14(b)(2) in its March 14, 2019, Final Confidentiality Determination letter. If Congress had intended to require EPA to disclose all information contained within or underlying health and safety studies, it would have used the word "shall" or "must." TSCA section 14(b)(1) provides that when confidential information is mixed with information that is not protected from disclosure, the confidential information does not lose its confidential status merely because it is contained within information that is otherwise disclosed. While the health and environmental results of a study can never be CBI, the underlying data that has commercial value can and should be protected from disclosure with EPA's discretion. EPA should amend its analysis and recognize that	EPA made the full studies available to peer reviewers and included a list of the studies and their results in the docket in accordance with TSCA section 26(j) and 40 CFR 702.51. Data quality evaluations for each study are available in the appendix and supplemental files. As discussed above, following substantiation of the CBI claims from the affected businesses, EPA has released fully unredacted or partially redacted versions of all of the studies discussed in the draft risk evaluation in the public docket for PV29 (EPA-HQ-OPPT-2018-0604). The Agency does not intend to amend its 2019 final confidentiality determination.

#	Summary of Comments for Specific Issues Related to Charge Question 1	EPA/OPPT Response
	TSCA section 14 provides EPA with discretion to protect CBI. (47_4) • Publishing confidential product data, such as valuable health and safety studies, would discourage companies from voluntarily expending resources on expensive toxicology studies. (19_22) • EPA's practice of protecting CBI in health and safety studies is consistent with past EPA practices and other chemical regulatory agencies around the world, including ECHA. (19_23) • Robust study summaries, as defined in the REACH regulation, provide "sufficient information to make an independent assessment of the study minimizing the need to consult the full study report." (19_24) • The SACC independent review minimizes the need to publicly release full study reports and provides the public with additional basis for confidence in the studies. (19_24)	
Update risk evaluation to reflect availability of studies that were previously redacted		
SACC	SACC COMMENTS: • Update the Evaluation to reflect recent changes in CBI availability. The Committee noted that there had been significant changes to CBI redacted information upon which the Draft Risk Evaluation relied. These formerly redacted studies are now publicly available for review.	EPA has updated the risk evaluation to reflect the public release of the studies with CBI claims.
Include description of the ramifications of the final risk statement		
SACC	SACC COMMENTS: • The Public needs to know that if a substance is determined to pose an "unreasonable risk," the Agency will address the identified risk(s) through	The final Risk Evaluation was modified to include detailed risk determinations for each condition of use in order to improve the understanding of the impact of the risk evaluation and if any risk management activities will follow the evaluation. Any

#	Summary of Comments for Specific Issues Related to Charge Question 1	EPA/OPPT Response
	a risk management process. At a minimum, reference should be made to Agency guidance on how this next step would proceed. • Any finding of no unreasonable risk is tied to limitations of currently available data and uses, including industrial hygiene practices, then the Evaluation should so state. A finding of "no unreasonable risk" should not preclude additional review. Substantial changes in use of the substance under review, and/or the development of new data that alters substantially knowledge of chemical properties, exposures and or toxicity, will alter exposures, toxicity, and will ultimately alter the overall risk. • The Committee expressed concerned that a finding of "no unreasonable risk" indicates to the public that nothing further will be done to evaluate or regulate the substance under review (in this case PV29). On the other hand, the prior designation of PV29 as a high priority chemical may suggest to many in the public that additional risk management measures will be enacted regardless of outcome. Additional clarification would be helpful so that manufacturers, state regulators, and the public will understand how the risk assessment finding will impact their current and future activity related to this substance. This statement is needed to clarify report findings and increase transparency of EPA intent following the report finding.	changes to risk determinations from the draft risk evaluation will be clearly stated. TSCA section 6 requires EPA to make a determination that a chemical substance undergoing risk evaluation presents or does not present an unreasonable risk of injury to health or the environment, under the conditions of use. In carrying out section 6, EPA must take into consideration information "that is reasonably available to the Administrator." TSCA section 26(k). A determination that a condition of use of a chemical substance does not present an unreasonable risk of injury is a final agency action. See TSCA section 6(i). Federal preemption of certain State actions regarding that chemical substance would apply only to the hazards, exposures, risks, and uses or conditions of use of such chemical substance included in that final agency action. See TSCA section 18(c)(3).

Systematic Review Approaches and Clarity

Charge Question 2.1: Please comment on the approaches and/or methods used to support and inform the gathering, screening, evaluation, and integration of information used in the draft risk evaluation of PV29 and the updated Pigment Violet 29 (81-33-4) Systematic Review: Supplemental File for the TSCA Risk Evaluation (Published April 17, 2019). Please also comment on the clarity of the information as presented related to systematic review and suggest improvements as it applies to PV29.

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
Need to describe the rationale for developing a systematic review method specific to TSCA		
SACC, 82	SACC COMMENTS: • Describe clearly the rationale for developing a systematic review specific to TSCA risk evaluations. • Describe clearly the rationale for the differences in the TSCA systematic review relative to other peer-reviewed systematic review approaches currently in use. **PUBLIC COMMENTS:** • EPA was not forthcoming during the SACC meeting when queried as to why it chose to develop its own method of systematic review for TSCA. (82_6)	EPA/OPPT's quality evaluation method was developed following identification and review of various published qualitative and quantitative scoring systems to inform EPA's specific fit-for-purpose tool. The development process involved reviewing various evaluation tools/frameworks (*e.g.*, OHAT Risk of Bias tool, CRED, etc.; see Appendix A of the *Application of Systematic Review in TSCA Risk Evaluations* document and references therein), as well as soliciting input from scientists based on their expert knowledge about evaluating various data/information sources specifically for risk assessment purposes. While EPA's/OPPT's systematic review process may differ from other procedures or guides, it was developed specifically for the TSCA risk evaluation process and included certain protocols and processes. Based on comments received and challenges experienced with EPA's/OPPT's process for the first round of risk evaluations, EPA is refining it systematic review process for added transparency and clarity. Additionally, the refinement process includes more detail, specificity, and data integration than previously applied as well as developing clearer, more transparent processes and practices to be applied in future risk evaluations. The refined systematic review process is being reviewed by the National Academy of Sciences.
Need to initiate an external peer review of the TSCA systematic review protocol		

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
SACC, 13, 16, 46, 48, 80, 82	**SACC COMMENTS:** • As soon as practical have NAS conduct a peer review of the TSCA systematic review protocol. **PUBLIC COMMENTS:** • EPA should immediately initiate an external, independent peer review of its TSCA systematic review protocol. Until external reviews are completed, EPA should not use the TSCA systematic review protocol. (13_242, 16_109, 46_25, 48_16, 80_1, 82_6)	An ad hoc committee of the National Academies of Sciences, Engineering, and Medicine is reviewing EPA's guidance document on *Application of Systematic Review in TSCA* [Toxic Substances and Control Act] Risk Evaluations (EPA 2018) and associated materials developed subsequent to its issuance. The committee is considering public comments on the document, EPA's responses to public comments, and enhancements to the systematic review process reflected in documentation of the first 10 chemical risk evaluations. The committee will determine whether EPA's process is comprehensive, workable, objective, and transparent. Recommendations for enhancements to EPA's 2018 guidance document will be made. More information and details about the NAS review effort are available here: https://www.nationalacademies.org/our-work/review-of-epas-tsca-systematic-review-guidance-document
Need to develop, peer review, and publish systematic review protocols prior to conducting TSCA risk assessments		
SACC, 13, 43	SACC COMMENTS: • Develop, peer review and publish SRs for substances undergoing TSCA risk assessment prior to conducting the actual risk assessment. **PUBLIC COMMENTS:** • EPA failed to establish an upfront protocol for PV29, which violates a basic principle of systematic review under TSCA. Developing systematic review protocols for each chemical in advance reduces bias and ensures transparency in decision-making. (13_217, 43_4) • Insufficient time is not an acceptable justification for EPA's failure to develop protocols. (13_221) • The systematic review protocols should be available and subject to public comment prior to	Systematic review and evaluation of reasonably available data for a chemical substance forms a major part of the risk evaluation process. In the interest of meeting the statutory deadlines set forth under TSCA for the completion of the risk evaluations, the systematic review process was conducted as the risk evaluations were being developed. To address systematic review best practices, EPA developed criteria for screening and evaluating reasonably available information before these specific systematic review processes occurred. For future risk evaluations, EPA will work to implement procedures to identify and fill critical data deficiencies at the beginning of the risk assessment process. EPA/OPPT's systematic review and data quality evaluation methods were developed in part by consulting various published qualitative and quantitative scoring systems. The development process involved reviewing various evaluation

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
	initiating subsequent steps of the risk evaluation process. (13_221)	tools/frameworks (*e.g.*, OHAT Risk of Bias tool, CRED, etc.; see Appendix A of the *Application of Systematic Review in TSCA Risk Evaluations* document and references therein), as well as soliciting input from scientists based on their expert knowledge about evaluating various data/information sources specifically for risk assessment purposes. Based on comments received and challenges experienced with EPA's/OPPT's process for the first round of risk evaluations, EPA is revising it systematic review process for added transparency and clarity. Additionally, the revision process includes more detail, specificity, and data integration than previously applied as well as developing clearer, more transparent protocols and practices to be applied in future risk evaluation processes. The revised systematic review process also went through a National Academy of Sciences in August, 2020. The recommendations resulting from this review are being summarized and will be made publicly available and incorporated into the process as needed.
Concerns that the TSCA systematic review method does not follow best scientific practices and should be replaced		
9, 13, 14, 16, 18, 43, 44, 46, 48, 55, 80	PUBLIC COMMENTS: • The TSCA systematic review method does not follow best scientific practices for systematic reviews. (9_5, 13_222, 14_2, 16_2, 43_1, 44_20, 46_12, 48_1, 55_4, 80_1) • Another example is that EPA has adopted a rigid, numerical scoring approach with weighted metrics to grade the quality of studies while other systematic review systems holistically evaluate and compare different studies and data sources, without relying on numeric scores. The National Academy of Sciences has cautioned against the use of scores	EPA will work with the National Academy of Sciences, Engineering, and Medicine (NASEM) TSCA Committee to consider revisions to the data quality evaluation criteria and options regarding integrating evidence within and across evidence streams (human, animal, mechanistic data). EPA proposes to use a more structured framework for evidence integration for the next set of chemicals evaluated under TSCA. Appendix A of the *Application of Systematic Review in TSCA Risk Evaluations* explains the basis for EPA/OPPT's development of a numerical scoring system to inform the characterization of the data/information sources during the data integration phase. The intent is to provide transparency and consistency to the evaluation process along with creating

	in systematic review. (13_10, 16_107, 44_20, 46_23, 48_14) • The TSCA approach focuses on one limited aspect of systematic review, study quality, but fails to address other critical elements that the Agency itself recognizes are essential for science-based risk judgments, such as identifying and evaluating each stream of evidence and integrating evidence as necessary and appropriate based on strengths, limitations, and relevance. (16_107) • EPA should use a peer-reviewed, validated systematic review method for chemical evaluations instead of the TSCA method even if that delays development and completion of some risk evaluations. Examples include the NTP Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration; the EPA Handbook for Developing IRIS Assessments; the Preamble to the IARC Monographs; and the Navigation Guide Systematic Review Method (Woodruff and Sutton, 2014). (13_313, 43_1, 48_16, 55_16) • Unlike the aforementioned approaches to systematic review, the TSCA protocol fails to address the steps TSCA risk evaluations will take to determine the strengths and relevance of individual studies, group them into streams of evidence and integrate these streams into a set of judgments about the weight of the evidence as a whole. (18_14)	evaluation strategies that meet the TSCA science standards for various data/information streams. EPA/OPPT's quality evaluation method was developed following identification and review of various published qualitative and quantitative scoring systems to inform our own fit-for-purpose tool. The development process involved reviewing various evaluation tools/frameworks (*e.g.*, NTP's Office of Health Assessment and Translation (OHAT) Risk of Bias tool, Criteria for Reporting and Evaluating Ecotoxicity Data (CRED), etc.; see Table 1 and Appendix A of the *Application of Systematic Review in TSCA Risk Evaluations* and references therein), as well as soliciting input from scientists based on their expert knowledge about evaluating various data/information sources for risk assessment purposes. While there are many published systematic review tools available for human health and environmental health hazard assessment, no systematic review tools were identified that encompass either exposure assessment (*e.g.*, general population exposures, occupational exposures and industrial releases) or fate and transport assessment. The published data quality evaluation results provided the lists of references EPA/OPPT evaluated for the first 10 TSCA risk evaluations. In order to ascertain the quality of the available data, EPA/OPPT used a numerical scoring system to assign a qualitative rating. The goal of this approach was to add consistency and transparency to the evaluation process. Scores were used for the purpose of assigning the confidence level rating of High, Medium, Low, or Unacceptable, and informed the characterization of data/information sources during the data integration phase. The data quality evaluation results for the first ten TSCA Risk Evaluations are posted on chemical specific websites (see Table 1). In all evaluation strategies, professional judgment was employed to determine the adequacy or appropriateness of the qualitative rating assigned by the numerical scoring system.

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
		The TSCA evaluation strategies consider methodological design and implementation and reporting within the existing domains and metrics. Since it is difficult to have high confidence in data where the underlying methods are unreported or poorly reported, EPA assesses reporting and methodological quality simultaneously. However, EPA recognizes the challenge of discerning between a deficit in reporting and a problem in the underlying methodological quality of the data/information source. Developing a reporting checklist, guidance document or a separate reporting quality domain may be a future solution for consideration in optimizing the evaluation strategies. EPA also designed evaluation criteria that consider risk of bias and Bradford Hill aspects when assessing the quality of animal toxicity and epidemiological studies. Refer to Appendices F, G and H of the *Application of Systematic Review in TSCA Risk Evaluations* for more information. EPA will consider other existing approaches as part of the process of developing the methods and/or approaches for integrating exposure and hazard evidence supporting the TSCA risk evaluations. Due to the variety of chemicals being evaluated under TSCA, EPA expects variations in the integration methods and/or approaches across different evidence streams as part of the process of developing fit-for-purpose risk evaluations that meet the TSCA science standards.
Need to more clearly describe the systematic review protocol and procedures		
SACC	SACC COMMENTS: • Describe clearly the explicit populations, exposures, comparators, and operators (PECO or	According to the *Application of Systematic Review in TSCA Risk Evaluations* U.S. EPA (2018a), systematic reviews typically describe the study eligibility criteria in the form of PECO statements or a modified framework. PECO stands for Population, Exposure, Comparator and Outcome. The

	problem formulation) used in the systematic review. • Describe clearly how the TSCA systematic review is updated and describe the rationale for decisions applied in the systematic review for specific substances.	approach is used to formulate explicit and detailed criteria about those characteristics in the publication that should be present in order to be eligible for inclusion in the review (*e.g.*, inclusion of studies reporting on the effects of chemical exposure to potentially exposed or susceptible subpopulations). EPA developed PECO statements to guide the screening of the environmental and human health hazard data or information sources for each of the TSCA risk evaluations. However similar guides for screening were developed for data and information of different disciplines using generic RESO and PESO statements. In the case of C.I. Pigment Violet 29, EPA did not exclude and populations, exposures, comparators or operators during the data search and screening process for C.I. Pigment Violet 29. Various PECO or PECO equivalent documents have been created to document the eligibility criteria for various data or information streams informing the TSCA risk evaluations: physical chemical properties; environmental fate and transport; engineering and occupational exposure; exposure to the environment, the general population and consumers; and environmental and human health hazards. It is important to mention that PECO/RESO/PESO statements can be modified once they are drafted and implemented, through a calibration process. Calibration is when screeners jointly screen 10-40 studies to identify points of confusion or chemical-specific considerations. More information about the use of specific populations used in the systematic review of PV29 are outlined in the *Application of Systematic Review in TSCA Risk Evaluations* available at:

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		https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf EPA anticipates feedback from the NAS on its systematic review process and will carefully review and implement relevant NAS recommendations, as appropriate.
Need to provide a more thorough discussion of data integration		
SACC, 8, 13, 48, 55	SACC COMMENTS: • Include a more thorough and inclusive data integration discussion in the TSCA systematic review for PV29. The discussion should include descriptions of how the human health experience, mechanistic information, in vitro data, and controlled laboratory animal data are used to support conclusions. Include in the discussion how chemical structural considerations, read across, and other information including finding from New Approach Methodologies (NAMs) add to the evidence for potential PV29 toxicity. The discussion should also address data uncertainties. PUBLIC COMMENTS: • The TSCA systematic review protocol does not include methods for evidence synthesis and integration as required by EPA regulation under TSCA. (48_14, 55_15) • The draft risk evaluation simply states that "EPA analyzed and synthesized" available evidence, without specifying its strategy for data integration. The discussion does not detail how individual	EPA appreciates the comments and is currently in the process of updating its Systematic Review protocol. In addition, EPA is seeking feedback from the National Academies of Science (NAS) on its Systematic Review process, including data evaluation criteria and data quality rating methods used in TSCA Risk Evaluations. The NAS webinars occurred from June through August, 2020. EPA will consider all comments and feedback received in updating its Protocol. In response to comments, EPA has made several editorial changes in multiple sections within the final Risk Evaluation document to increase the transparency of its systematic review process and methodologies used. In addition to the data evaluation criteria published in the *Application of Systematic Review in TSCA Risk Evaluations*, EPA has updated the systematic review components of the final Risk Evaluation which revises or adds data quality evaluation reviews for all available data for human health, environmental hazard, environmental fate, physical chemical property data, environmental release occupational exposure data quality evaluation reviews in the assessment. The updated systematic review scoring sheets, released on April 17, 2019 (EPA-HQ-OPPT-2018-0604-0040) with updated data quality evaluation scores and reviewer comments, are reflected in Systematic Review Companion Documents released with the final Risk Evaluation. EPA is developing

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
	study scores were used in this step of the review process for PV29. (13_234) • EPA should describe its general approach to evidence integration, referring to established systematic review approaches. (13_235) • If OPPT relied directly on SAR evaluations or other data used in international agency assessments of PV29, OPPT should indicate this and describe how the other evaluations were evaluated to determine their robustness. (8_16)	and implementing more formal and structured data integration, analysis and synthesis strategies for the next set of TSCA chemical risk evaluations. There EPA utilized SAR tools in its assessment, EPA evaluated these tools for data quality. The results of the data quality evaluation of the EPIsuite™ modeling program is available in the supplemental file, *Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies*" U.S. EPA (2020b)
Insufficient data concerns and handling of lack of data		

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
SACC, 10, 12, 13, 15, 16, 18, 44, 46, 49, 82	SACC COMMENTS: • Discuss why an "indeterminate" designation is not needed in the TSCA systematic review to account for situations where there is significant lack of data. • Improve the discussion on why available study data are adequate to reach the conclusions of "no *unreasonable* risk" from exposure to PV29. This discussion should also justify why additional testing is not necessary to confirm this conclusion. PUBLIC COMMENTS: • The systematic review did not gather all appropriate data and EPA should use its authorities under TSCA to obtain additional information. (10_13, 12_3, 13_73, 15_22, 16_13, 18_5, 44_5, 46_1, 49_2, 82_2) • The updated study quality scores for the two BASF acute inhalation toxicity studies as Unacceptable further highlights the lack of sufficient information available to evaluate PV29's risks. (13_227, 46_14) • EPA did not include a review of, or reference to, a 90-day repeated dose dietary study in rats that also is in the REACH database for this chemical. (49_4)	In response to uncertainties resulting from lack of data identified in public and SACC comments, as well as in the risk evaluation, EPA issued a TSCA Section 4(a)(2) Test Order for PV29 on February 28, 2020. The Test Order was issued to the one U.S. manufacturer, Sun Chemical Corporation, and one U.S. importer, BASF, and required the generation and submission of three studies to address critical data gaps identified in the risk evaluation. More information about the Section 4 Test Order for PV29 can be found in the docket (EPA-HQ-OPPT-2020-0070-0008). EPA is currently developing a procedure to identify data deficiencies earlier in the risk evaluation process so an indeterminate designation is not necessary. As indicated above, EPA issued a TSCA Section 4(a)(2) Test Order for PV29 on February 28, 2020 to the one U.S. manufacturer, Sun Chemical Corporation, and one U.S. importer, BASF, that required the generation and submission of three studies to address critical data gaps identified in the risk evaluation. More information on this Test Order can be found on its docket (EPA-HQ-OPPT-2020-0070-0008). In the absence of reasonably available data to characterize inhalation toxicity of PV29, EPA has used analog toxicity data to characterize the risks to human health from occupational exposure to PV29. EPA did not identify a US data owner for these studies. As the full study reports could not be obtained for these study summaries, EPA did not utilize the results in the assessment, although they appeared to be consistent with the Reproduction/ Developmental Toxicity Screening Test discussed in the assessment.
Concerns about the quality of the body of evidence for PV29		

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
43, 47, 48, 55	PUBLIC COMMENTS: • Applying the Navigation Guide risk of bias tool to the 15 PV29 animal toxicity studies indicates that the overall quality of the body of evidence is low. (43_7, 48_11, 55_13) • Based on the partial disclosure of reports of the 24 PV29 studies, the limitations and deficiencies of these studies in assessing PV29's acute and chronic health effects have been further demonstrated, providing more evidence that EPA's lacks any justification for its conclusion that PV29 "presents a low hazard to human health across all routes of exposure". (47_2)	All studies and information used in the Risk Evaluation, including those submitted through correspondences with manufacturing stakeholders of PV29, are evaluated using the same data quality criteria under the TSCA Systematic Review process described in the document, *Application of Systematic Review in TSCA Risk Evaluations*. In consideration of comments received, EPA is in the process of updating the TSCA Systematic Review protocol to improve the transparency of this review process and further reduce possible bias such that all studies are appropriately considered. As indicated in the final Risk Evaluation, EPA issued a TSCA Section 4(a)(2) Test Order for C.I. Pigment Violet 29 on February 28, 2020. This test order compelled the creation and submission of three studies by the sole US manufacturer of PV29, Sun Chemical, as well as BASF, an importer of PV29 to address critical data gaps identified in the risk evaluation. In an effort to increase transparency, EPA has released all data that were used to conduct the risk evaluation, with some redactions for CBI. CBI in several study reports prevented the release of fully unredacted versions of these studies. Fully unredacted versions of these studies were made available to the SACC members and their input on the quality of the studies and the effect of the remaining redactions on the ability of the general public to interpret the studies was recorded in the *Transmittal of Meeting Minutes and Final Report for the TSCA Science Advisory Committee on Chemicals Meeting Held June 18-21, 2019*, which was made available in the public docket for PV29 (EPA-HQ-OPPT-2018-0604-0089).
Concerns relating to the personal communication from Sun Chemical		

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
SACC, 12, 13, 14, 15, 16, 17	SACC COMMENTS: • Perform a quality assessment of the exposure data for occupational exposures to PV29 that was provided to the Agency as a personal communication from the manufacturer of PV29. PUBLIC COMMENTS: • EPA's characterization of human health risk is based on the suspect and undocumented workplace exposure estimates privately provided to EPA by the chemical's manufacturer. (12_3, 13_8, 14_17, 15_10, 16_20) • EPA heavily and inappropriately relied upon unsubstantiated industry correspondence to inform its exposure analysis, but this correspondence was exempted from quality review under its systematic review approach. (13_236) • The Sun Chemical Corporation communication as reported by EPA fails to meet the minimal requirements for poor quality data, and it should be classified as unacceptable. (15_13) • This personal communication does not constitute the "best available science" showing worker exposures and it does not meet the scientific standards of industrial hygiene. Therefore, it cannot reasonably form the basis of EPA's conclusion that PV29 does not pose an unreasonable risk to workers. (12_12) • If EPA receives data from a manufacturer, the data should be reviewed for accuracy, quality, relevancy and suitability. EPA should specify how it evaluated these sources for PV29. (17_15)	As part of the final Risk Evaluation, EPA has conducted a data quality evaluation for all environmental release and occupational exposure data received for PV29 through correspondences with manufacturing stakeholders and has made this information publicly available in the companion document to the final Risk Evaluation titled, "*Supplemental File: Information Received from Manufacturing Stakeholders*." In cases where data were insufficient or inadequate to meet the minimum validity criteria, EPA has made efforts to clarify the information. In the case of occupational exposure data, EPA compelled the creation and submission of a workplace monitoring study of particle not otherwise regulated, conducted according to the NIOSH 0600 by the sole US manufacturer of PV29, Sun Chemical as well as BASF, an importer of PV29.
Need for public access to data		

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
SACC, 13, 46	SACC COMMENTS: • Ensure that Confidential Business Information (CBI) requirements do not prevent important health-based data from being made available to the public. PUBLIC COMMENTS: • Systematic review practices require access to full studies. The lack of study detail in the study summaries calls into question EPA's ability to reliably evaluate study quality. (13_24, 46_4) • EPA should make such information public and easily searchable through online portals such as the Health and Environmental Research Online (HERO) database. (13_24)	On March 21, 2019, EPA released copies of the 24 study reports claimed as CBI to the public docket for PV29 (EPA-HQ-OPPT-2018-0604). Fifteen study reports were completely released without redactions, while nine reports remain partially CBI with certain information redacted. As indicated above, on April 4th, 2019, EPA released an updated version of the systematic review documents for the PV29 risk evaluation. The systematic review materials for PV29 were updated following the release of study reports to include the reviewer's comments and a reevaluation of several human health studies (EPA-HQ-OPPT-2018-0604-0040). These updated systematic review data quality evaluation results were also released as supplemental documents to the final Risk Evaluation. EPA hopes that this enhances the transparency of the systematic review portion of the risk evaluation.
Study quality evaluation and scoring concerns		
SACC, 8, 13, 16, 17, 43, 46, 47, 48, 55	SACC COMMENTS: • Describe clearly the justification for using a weighted scoring system and the rationale for the metrics selected for differential weighting in its evaluation of studies. • Provide additional rationale to the TSCA systematic review justifying NR codes for certain metrics that are not typical of animal studies and improve discussions on how an NR code impacts the quality score. • Include data quality criteria in the TSCA systematic review for evaluating personal communications and other information types not already identified in the TSCA systematic review	Appendix A of the *Application of Systematic Review in TSCA Risk Evaluations* explains the basis for EPA/OPPT's development of a numerical scoring system to inform the characterization of the data/information sources during the data integration phase. The intent is to provide transparency and consistency to the evaluation process along with creating evaluation strategies that meet the TSCA science standards for various data/information streams. EPA/OPPT's quality evaluation method was developed following identification and review of various published qualitative and quantitative scoring systems to inform our own fit-for-purpose tool. The development process involved reviewing various evaluation tools/frameworks (*e.g.*, NTP's Office of Health Assessment and Translation (OHAT) Risk of Bias tool, Criteria for Reporting and Evaluating Ecotoxicity Data (CRED), etc.; see Table 1 and Appendix A

	that might be considered critical in a risk evaluation. PUBLIC COMMENTS: • The numerical scoring approach was not effective for evaluating study flaws. Overall scores can mask flaws that might otherwise cause a study's conclusions to be questioned. (13_222) • The scoring system could result in many studies being arbitrarily classified as "poor" or "unacceptable" based on a small number of reporting or methodology limitations that do not negate their overall value for assessing health risks. (16_107) • The study quality scoring system is highly questionable in the absence of any external validation phase or thorough pilot testing. (48_11) • EPA should provide more explicit criteria and descriptions for the Not Rated/Applicable score determination. (46_20) • There were many changes in the study quality metric ratings for the animal toxicity studies between the initially released and updated systematic review documents. This suggests the criteria for the metrics are not clear and it reveals numerous inconsistencies and inaccuracies in the scoring sheets. (43_4, 46_21, 48_11) • It appears that different reviewers were used for the second round of scoring than the first, suggesting that the scores depend heavily on the subjective judgement of the reviewer. (48_11, 55_11) • It seems that there was one reviewer for each study, although best scientific practice is to have two independent reviewers. (43_6, 46_22, 48_11) • The scoring sheets provide the quality scores but do not provide information regarding the rationale for scores. EPA should make the reviewer	of the Application of Systematic Review in TSCA Risk Evaluations and references therein), as well as soliciting input from scientists based on their expert knowledge about evaluating various data/information sources for risk assessment purposes. While there are many published systematic review tools available for human health and environmental health hazard assessment, no systematic review tools were identified that encompass either exposure assessment (*e.g.*, general population exposures, occupational exposures and industrial releases) or fate and transport assessment. The data quality evaluation results published with each risk evaluation provides the lists of references EPA/OPPT evaluated for the first 10 TSCA risk evaluations. In order to ascertain the quality of the available data, EPA/OPPT used a numerical scoring system to assign a qualitative rating. The goal of this approach was to add consistency and transparency to the evaluation process. Scores were used for the purpose of assigning the confidence level rating of High, Medium, Low, or Unacceptable, and informed the characterization of data/information sources during the data integration phase. The data quality evaluation results for the first ten TSCA Risk Evaluations are posted on chemical specific websites. In all evaluation strategies, professional judgment was employed to determine the adequacy or appropriateness of the qualitative rating assigned by the numerical scoring system. The TSCA data evaluation strategies consider methodological design and implementation and reporting within the existing domains and metrics. Since it is difficult to have high confidence in data where the underlying methods are unreported or poorly reported, EPA assesses reporting and methodological quality simultaneously. However, EPA recognizes the challenge of discerning between a deficit in reporting and a problem in the

	comments publicly available or provide more detail on the rationales behind the scores. (8_11, 13_6, 17_14) • EPA should continue to update its systematic review guidance to provide greater clarity and transparency in regard to study quality criteria. It remains unclear how EPA will address the quality of more disparate study types that may be encountered for other chemistries. (8_5, 47_3) • EPA must ensure that its scientists and contractors are appropriately trained and equipped and given the scientific independence to conduct robust evaluations of study quality. (46_12) • EPA had failed to empirically document the link between its scoring metrics and the overall value of a study in a holistic evaluation of risk. (48_12)	underlying methodological quality of the data/information source. Developing a reporting checklist, guidance document or a separate reporting quality domain may be a future solution for consideration in optimizing the evaluation strategies. EPA also designed evaluation criteria that consider risk of bias and Bradford Hill aspects when assessing the quality of animal toxicity and epidemiological studies. Refer to Appendices F, G and H of the Application of Systematic Review in TSCA Risk Evaluations for more information. Relevant data sources are evaluated for data quality following title/abstract and full-text screenings, after a pilot period to calibrate criteria and revise as needed. Generally, each study evaluation is conducted by at least two reviewers, with a process for comparing and resolving differences. This helps ensure quality assurance. However, based on assessment needs, the assessment team should make decisions about how many reviewers are needed. While more than one reviewer is ideal, there may be times when one reviewer is acceptable, such as when the assessment needs to be conducted under a rapid timeframe and the outcome being reviewed is unlikely to be a driver for the assessment. These quality assurance methods are the same as used by EPA's IRIS Program. Other EPA Offices (such as Office of Research and Development and the Office of Science Coordination and Policy) partnered with OPPT in developing innovations in searching and screening for the next 20 chemical evaluations (see response to Q5) and continue to support OPPT in scoping and SR efforts. The data evaluation is conducted in a tool (*e.g.*, Excel, Access, DistillerSR) that tracks and records the evaluation for each data/information source including reviewer's comments. EPA initially released the SR Supplemental File without the EPA reviewer's comments due to concerns that

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
		the comments might contain information claimed CBI. The Updated SR Supplemental File, released on April 4, 2019, now makes publicly available the EPA reviewer's comments related to the data quality evaluation of the physical chemical characteristics, environmental fate, environmental hazard and human health studies (EPA-HQ-OPPT-2018-0604-0040). EPA will make reviewer comments public with the release of the Systematic Review Companion documents for the final Risk Evaluation to increase transparency. This documentation approach also increased transparency of professional judgment calls to stakeholders and the public for the first 10 TSCA risk evaluations. EPA/OPPT plans to use these evaluation strategies, including pre-determined criteria, documented in EPA's Application of Systematic Review in TSCA Risk Evaluations document, for the next 20 TSCA risk evaluations. However, refinements to the evaluation strategies are likely to occur. EPA already made changes to the physical chemical properties, environmental hazard, and epidemiological criteria since the Application of Systematic Review in TSCA Risk Evaluations document was published. These changes were due to validation and improvement efforts to ensure that the most relevant studies were included in the TSCA risk evaluations, and the most up-to-date data quality evaluation criteria are used for the next 20 TSCA risk evaluations. Use of an NR rating for a score is up to the scientific judgement of the reviewer. This rating should be applied when the metric or domain is not relevant to the scoring criteria. If this rating of NR is applied, then the metric is not counted towards the overall data quality evaluation score of the study.
TSCA systematic review method was effective for PV29		

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
8, 17, 19, 47	PUBLIC COMMENTS: • EPA appropriately gathered and considered all of the available and relevant data for PV29. (8_9, 17_17, 19_11) • EPA's use of data generated for other regulatory programs is important and encouraged. (17_7) • EPA completed a thorough review to verify the quality of the submitted studies. (19_11) • ACC commends EPA on its approach to using inhalation exposure data provided by a manufacturer as a means to obtain useful data in an expedient manner. (17_17) • The updated systematic review increased transparency in regard to study quality evaluation and is a marked improvement over EPA's original PV29 systematic review document. (47_1)	EPA acknowledges these comments and has made no change
Include discussion of toxicity of byproducts of manufacturing and impurities in PV29		
SACC, 12, 13, 46	**SACC COMMENT**: • Include a discussion on the potential toxicity of byproducts of manufacturing and impurities in PV29. PUBLIC COMMENT: • EPA did not review studies on chemical residuals of the PV29 manufacturing process. (12_26, 46_6) • In the problem formulation, EPA identifies naphthalimide as a residual of PV29 as manufactured. Workers are potentially exposed to naphthalimide. EPA has dropped all mention of this chemical in the draft risk evaluation. EPA must conduct a much more extensive review of the extent of presence and the potential risks of naphthalimide in PV29 before reaching a decision	EPA's exclusion of naphthalimide impurities of reactions in the production of other chemicals from the scope of this risk evaluation is a policy decision. In exercising its discretion under section 6(b)(4)(D) to identify the conditions of use that EPA expects to consider in a risk evaluation, EPA believes it is important for the Agency to have the discretion to make reasonable, technically sound scoping decisions. EPA anticipates that any risks presented by the presence of naphthalimide impurities will be considered in the scope of any risk evaluation of those chemicals. EPA believes that, rather than evaluate one aspect of the risk that may be presented by naphthalimide, a more sensible approach is to consider that risk while evaluating the risks that may be presented by the naphthalimide itself. Naphthalimide generated as a byproduct of the production of PV29 is outside the scope of this risk evaluation. EPA believes that

#	Summary of Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
	to do no further analysis. (12_26, 13_213-215, 46_6)	its regulatory tools under TSCA section 6(a) are better suited to addressing any unreasonable risks that might arise from naphthalimide as a byproduct of the production of PV29.

Physical Chemical Properties and Environmental Fate

Charge Question 3.a: Please comment on the characterization of Log Kow, Koc and bioaccumulation for PV29, including any suggestions for alternative sources or methods to obtain or derive better estimates of the properties (*e.g.*, use of specific analogs).

Charge Question 3.b: Please comment on characterization of the physical chemical properties of PV29, especially with regard to the determination by the European Chemicals Agency (ECHA) to include PV29 on the 2019-2021 Community Rolling Action Plan (CoRAP) update as a "suspected PBT/vPvB [Potentially Persistent, Bioaccumulative and Toxic/very Persistent and very Bioaccumulative substance]." The CoRAP justification document for PV29 is available at: https://echa.europa.eu/documents/10162/13628/corap_justification_201-344-6_226-866-1_be_12079_en.pdf/cf312ff9-6b18-8b76-bc66-d86320faa24a

#	Summary of Comments for Specific Issues Related to Charge Question 3	EPA/OPPT Response
Concerns about water solubility study and value EPA used		
13, 45, 55, 78	PUBLIC COMMENTS: • EPA did not explain why the water solubility value provided in the 2017 PV29 scoping document was discarded in the draft risk evaluation. (13_38) • The study used to determine water solubility failed to consider pH and its influence on water solubility. (13_37) • Measured values for relatively poorly soluble substances are highly uncertain. (13_41) • EPA used an incomplete data set and selected lowest solubility estimate available. (78_6) • While the water solubility estimate is higher than the actual measured solubility for PV29, it is still more than 10 times lower than the estimate provided in the CoRAP Justification Document. (45_15) • The CoRAP Justification Document failed to incorporate the output of the most recent EPA ECOSAR estimation program. (45_16) • Studies provided in the ECHA dossier for PV29 reported higher solubility values. (13_39, 55_17)	The structure of PV29 is unique. Not only does it have the chromophore to give its color, it is also entirely planar and has multiple hydrogen bonding groups to give it high stability. The highly symmetric nature of the structure allows for efficient molecular packing and strong intermolecular hydrogen bonding at both ends to give a closely packed herringbone or stair-step type manner. As a result, the substance has a very high melting point (> 500 deg C) for an organic substance and low water solubility. The value that was 16.9 times higher was inconsistent with the expected solubility due to its highly stable intermolecular structure. The value from EPI allows for the input of a melting point value. The standard protocol values EPA reports include the water solubility. The water solubility test guidelines call for testing the substance in deionized water and recording the pH of the test solution during the test. The study performed by BASF determined the pH to be 6 during the water solubility study. Also, it should be noted that PV 29 was found to be insoluble in most solvents except for concentrated sulfuric acid which was used to perform the UV studies. Therefore,

#	Summary of Comments for Specific Issues Related to Charge Question 3	EPA/OPPT Response
		the substance is soluble under highly acidic conditions (though the exact value was not determined). EPA issued a test order to require the sole manufacturer of PV29 to submit additional testing to measure the solubility of PV29 in water and octanol. The results of this testing are incorporated into the final Risk Evaluation. This testing was conducted with a modified protocol that accommodates the particular physical-chemical characteristics of PV29 and EPA has high confidence in the study results.
Remove statements that low aqueous solubility precludes oral bioavailability		
SACC	SACC COMMENTS: • Remove statements that claim that an aqueous solubility of ≤ 11 µg/L precludes oral bioavailability.	EPA has updated the final Risk Evaluation to remove these statements.
Use alternative methods to generate information to evaluate bioavailability		
SACC	SACC COMMENTS: • Use alternative property estimation methods to generate the additional information needed to strengthen the weight of evidence to conclude that PV29 is not bioavailable.	EPA has utilized several in-silico methods to strengthen the available body of evidence that discusses the bioavailability of PV29 where possible.
Concerns about use of EPI Suite™		

#	Summary of Comments for Specific Issues Related to Charge Question 3	EPA/OPPT Response
SACC, 13, 45	PUBLIC COMMENTS: • EPA should clarify and address the appropriateness of using EPI Suite estimates in evaluating PV29's risks. (13_52) • EPA altered its prior characterization questioning the reliability of estimates derived using EPI (Estimation Programs Interface) Suite™. (13_53) • Using modelled estimations for water solubility from EPI Suite is inconsistent with the REACH guidance. (45_1) • Significant problems remain with EPI Suite, but versions linked to the PBT Profiler were improved in their accuracy with respect to organic pigments. (45_12) • Models like EPI Suite historically have tended to predict a much higher solubility than experimental results determine for substances outside the calibration range of the models. (45_13)	In the absence of measured data, estimating chemical properties can be used to obtain approximate values to get an idea of the chemical behavior. The model limitations should be taken into consideration when evaluating the results. For PV29, the chemical substance does not contain structural elements that would lead EPA to believe that the model would not provide a good estimated value. As discussed in the assessment, Log K_{OW} is not a relevant property for PV29 because it demonstrates a low solubility in octanol and water and behaves more like an insoluble particle. As such, it is not expected to absorb into organisms or tissues. As discussed above, EPA has required the submission of measured data to characterize the solubility of PV29 in water and octanol. Therefore, the result of this testing was utilized in the final Risk Evaluation. EPA routinely relies on modeled predictions of physical chemical properties when measured values cannot be obtained due to the nature of the substance. PBT Profiler is no longer available at the EPA web site. Fate and transport data extracted from the Systematic Review and submitted testing reports were used as the base of PV29's fate assessment. EPA required the development and submission of measured data to characterize the solubility of PV29 in water and octanol. While EPA chose to rely on the measured solubility data, a comparison with these values and the EPI-estimated solubility values (estimated to be 0.01 mg/L with an input of 400 deg C as the Melting Point and 0.001 mg/L with an input of 500 deg C) indicates that EPI-estimated values were

#	Summary of Comments for Specific Issues Related to Charge Question 3	EPA/OPPT Response
		higher than the measured values, but still indicates low water solubility.
Lack of clarity and data to support conclusions regarding bioaccumulation potential		
13, 16	PUBLIC COMMENTS: • EPA did not indicate the methods used in deriving its BAF and BCF values. (13_49) • EPA relies on incomplete and uncertain data to conclude that PV29 does not bioaccumulate. (13_46) • The evidence for solubility and bio-accumulation potential is inconclusive. (16_45, 16_62)	The solubilities of PV29 in both water and Octanol were confirmed by EPA from recent studies submitted by Sun Corporation under the TSCA section 4 order. Therefore, the BCF and BAF values calculated by EPI Suite using estimated Kow value will not be used in the final PV29 Risk Evaluation.
Supportive of conclusion that PV29 is poorly absorbed		
19, 45	PUBLIC COMMENTS: • Based on physicochemical properties of PV29, EPA correctly classified PV29 as poorly absorbed by all routes of exposure. (19_7) • Measured values for octanol and water solubility using the ETAD method, which were submitted to ECHA under science-based guidance adopted by ECHA for assessments under REACH, and submitted to EPA for its Draft Risk Evaluation, accurately indicate that PV29 is not bioaccumulative. (45_1)	EPA classified PV29 as poorly absorbed because of the low solubility and the relatively large molecular weight, which hinders PV29's particles ability to penetrate through membranes.
Ensure consistency or justify differences among physicochemical properties across the assessment		
SACC	SACC COMMENTS: • Ensure that the physical-chemical properties used throughout the Evaluation are consistent or note the reasons for discrepancies.	EPA has reviewed the physical chemical properties used throughout the document for consistency
Consider metabolic pathway prediction software to identify intermediates		

#	Summary of Comments for Specific Issues Related to Charge Question 3	EPA/OPPT Response
SACC	SACC COMMENTS: • Consider using metabolic pathway prediction software to look for potentially problematic intermediates for PV29. Despite the fact that PV29 seems to have minimal ready biodegradation, the production of toxic and persistent metabolites is always a concern especially for any compound having structure similar to PAHs. • Develop and justify high-quality estimates for log K_{ow} or fat solubility to solidify the argument that PV29 is not bioavailable or likely to be absorbed into organisms or tissues. • Improve the discussion supporting the importance of K_{oa} and better illustrate its implications on determinations of environmental distribution of PV29 and resulting exposure to humans and other organisms.	The lack of biodegradation and low solubility of PV29 in water and octanol means that the chemical is out of the bounds of the metabolic prediction software. In addition, PV29 is not expected to be metabolized due to low potential for absorption, so the production of metabolites is not expected. As discussed in the assessment, LogK_{OW} is not a relevant property for PV29 because it demonstrates a low solubility in octanol and water and behaves more like an insoluble particle. As such, it is not expected to absorb into organisms or tissues. EPA issued a test rule Order under TSCA section 4(a)(2) requiring the Sun Chemical Corporation and BASF to conduct solubility testing for PV29. These tests were required to address the uncertainties identified by EPA and members of the Science Advisory Committee on Chemicals (SACC) regarding PV29's water and octanol solubility. EPA issued this test rule Order because, for an insoluble particulate substance such as PV29, the octanol and water solubility should be considered separately to give a useful estimate for the Log K_{ow} and an indication of its bioavailability. The Sun Chemical Corporation conducted these studies under protocols reviewed by EPA and based on OECD Test No. 105 for water solubility and the Ecological and Toxicological Association of Dyes and Organic Pigments (ETAD) method for octanol solubility. The study results, which are available on regulations.gov at (EPA-HQ-OPPT-2020-0070-0008), were conducted under Good Laboratory Practices according to provisions in 40 CFR part 792. The solubilities were determined for PV29 after being ground into a fine powder and mixed in water or octanol for 24, 48, or 72 hours at room temperature. To determine the

#	Summary of Comments for Specific Issues Related to Charge Question 3	EPA/OPPT Response
		concentration of PV29 dissolved in water or octanol, samples were passed through filters to remove any suspended PV29 particles. The concentration of PV29 dissolved in water or octanol was below the analytical quantitation limit of 0.003 mg/L in every sample tested. These studies confirm that PV29 is an insoluble particulate substance and there is no expectation that PV29 will be taken up by fat solubility. The octanol-air partitioning coefficient (Koa) describes the distribution of a substance between octanol and air. The results of the octanol solubility experiment, where PV29 was not detected in any sample above the analytical quantitation limit of 0.003 mg/L, demonstrates that PV29 does not dissolve in octanol. Therefore, there is no expectation that PV29 will be taken up by terrestrial organisms through fat solubility.
Concerns about environmental persistence and fate evaluation and lack of data		
SACC, 13, 55	SACC COMMENT: • Projection of environmental fate based on one-at-a-time examination of physical properties is unscientific. PUBLIC COMMENTS: • EPA downplays the level of environmental persistence for PV29. (13_44) • The Belgian Competent Authority issued a document that elaborates on why PV29 should be considered a potential PBT, observing that "[i]n view of the structure of the substances, it is reasonable to expect that the persistent and the very persistent criterion are met for these substances and QSAR estimations support this concern." The Document adds that, for bioaccumulation potential,	EPA issued a Section 4 Test Order to require the manufacturer of PV29, as well as an imported to generate and submit additional testing to measure the solubility of PV29 in water and octanol (more information can be found in the Test Order docket (EPA-HQ-OPPT-2020-0070-0008). The results of this testing are incorporated into the final Risk Evaluation. This testing was conducted with a modified protocol that accommodates the particular physical-chemical characteristics of PV29 and was determined to be high quality after review with the data quality evaluation criteria for physical chemical property studies Nicolaou (2020). The results of the data quality evaluation of the physical chemical property studies can be found in the supplemental file, "*Systematic Review Supplemental File: Data Quality Evaluation of Physical-Chemical Property Studies* U.S. EPA (2020c)." EPA also identified articles on similar organic

#	Summary of Comments for Specific Issues Related to Charge Question 3	EPA/OPPT Response
	"the log Kow and log Koa-values are important metrics" and indicate a "high potential for bioaccumulation in air breathers" and that "the substance may accumulate in terrestrial organisms and in mammals. The Document underscores that significant additional testing is needed to better define PV29's P and B properties, in marked contrast to the draft PV29 evaluation, which presumes that PV29 is not a PBT based on the data available. (55_17)	pigments and used the research results as references to support EPA's fate assessment on PV29. EPA agrees with the assessment that PV29 is a persistent substance. The Belgian assessment relied on experimental results for Kow and Koa which EPA determined to be unacceptable. EPA issued a test rule Order and Sun Chemical Corporation conducted solubility testing showing that PV29 does not dissolve in octanol or water. Therefore, PV29 is considered not bioaccumulative for purposes of TSCA risk evaluation.

Exposure and Releases

Charge Question 4.a: Please comment on the characterization of occupational exposures (inhalation and dermal) for the manufacturing workers. Is the panel aware of other additional relevant information, including PV29 specific data, that could be considered?

Charge Question 4.b: Please comment on the environmental release characterization for the manufacturing and use as a site limited intermediate. Is the panel aware of other relevant additional information, if any, that could be considered?

Charge Question 4.c: Please comment on the exposure and release characterization for the downstream processors and users. Is the panel aware of other PV29 specific data and/or information that could be considered?

Charge Question 4.d: Please comment on the screening level approach used in the context of the conclusions associated with potentially exposed susceptible subpopulations (*e.g.*, to children, workers, or pregnant women). Please comment on other additional information or analyses that could be conducted, if any, in light of the screening level approach used in this case?

Charge Question 4.e: Please comment on the conclusion regarding the need for aggregate exposure.

#	Summary of Comments for Specific Issues Related to Charge Question 4	EPA/OPPT Response
Supportive of EPA's occupational exposure assessment		

#	Summary of Comments for Specific Issues Related to Charge Question 4	EPA/OPPT Response
17, 45	• The PV29 estimation of occupational exposure is evidence of the utility of EPA's risk assessment approach in appropriate cases. (17_4) • The current regulatory standards applicable to inert nuisance dusts such as PV29, as well as the limited U.S. production and use of the material, adequately restrict reasonably foreseeable worker exposures. (45_1)	EPA acknowledges these comments and encourages the commenters to consult the final Risk Evaluation to note changes to the occupational exposure.
Incorporate uncertainty analysis and screening-level fugacity modeling in life cycle safety assessment		
SACC	SACC CCOMMENTS: • Incorporate uncertainty analysis into the life cycle safety assessment (LCSA) risk evaluations and, at a minimum, present screening-level calculations when dismissing exposure pathways. • For non-ionizable organics, EPA should adopt a screening level fugacity modeling approach as a default under LCSA.	EPA included screening level occupational exposure estimates for processing and downstream users According to the developers of the fugacity model, for substances like PV29 with no solubility in octanol or air, this model may not be useful Mackay et al. (1996). This is because particulate substances like PV29 do not dissolve in water, air, or octanol like molecular chemicals. Instead, particulate substances will adsorb to solid surfaces and undergo particle transport rather than partition between air, water, and organic Mackay et al. (1996). To model particulate substances, EPA would need to determine the rates of attachment and detachment of PV29 particles to environmental surfaces. EPA, under TSCA, has not conducted such a modeling effort to date.
EPA did not consider full range of uses and exposure pathways		
12, 13, 17, 18	PUBLIC COMMENTS: • EPA failed to identify or evaluate PV29's full range of uses by ignoring many uses identified in the 2012 TSCA Work Plan and uses that other reliable sources consider "intended" and "reasonably foreseen." (12_8) • EPA has dismissed a wide range of uses for PV29 and erroneously suggests that its risk	TSCA Section 3(4) grants EPA the authority to determine what constitutes a condition of use for a particular chemical substance. In the case of PV29, there were a group of "other uses" that were identified early in the process with poor quality references. Subsequent to the publication of the scope document, no further information was found or received by EPA that substantiated any of the uses with limited and poor-quality references that had been characterized as "other uses".

	characterization should be limited to "actual use" of PV29. However, TSCA requires EPA to evaluate a chemical's risk under its conditions of use and reasonably foreseen conditions of use. Any circumstances that have been known to have occurred in the past are reasonably foreseen conditions of use and EPA must consider them in the risk evaluation. (13_59-68). • The risk characterization did not account for the full range of occupational uses and exposures. Workers are potentially exposed by multiple routes including dermal absorption, inhalation, and possibly oral ingestion. (12_16, 13_8, 18_16) • EPA must revise its evaluation to reflect all occupational uses and exposures, use its authority to collect data, and reissue for public comment. (18_16) • EPA lacks sufficient information to evaluate potential uses of PV29, including the likely duration, intensity, frequency, and number of exposures under all conditions of use. The omission of even a single condition of use is fatal to EPA's risk evaluation. (12_10, 13_187) • EPA has not fully evaluated conditions of use for consumers. (12_8, 13_244) • EPA has ignored reasonably foreseeable uses and uses with evidence that the use is occurring or has recently occurred, particularly with PV29 as an intermediate. (13_5, 13_59, 13_79) • EPA did not consider all relevant exposures under the conditions of use (*e.g.*, as an intermediate, import), as required under TSCA. Moreover, EPA's arguments for excluding certain conditions of use cannot simply be extended to exclude consideration of exposures and hazards (13_5, 13_6, 13_287, 13_244, 13_261).	As a result, these uses were determined to not be intended, known, or reasonably foreseen and are not conditions of use. EPA does not believe that it is appropriate to categorically consider all activities that occurred in the past but are not currently occurring to constitute reasonably foreseen conditions of use. As explained in the *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* rule preamble, 82 FR 33726, 33730-1 (July 20, 2017), "[i]t is reasonable to foresee a condition of use, for example, where facts suggest the activity is not only possible but, over time under proper conditions, probable." EPA's risk evaluation includes all known, intended, and reasonably foreseen conditions of use. During EPA's initial PV29 use investigation, a search was conducted to create the use document (EPA-HQ-OPPT-2016-0725-0004). This use document was not limited to only TSCA uses or information of a particular level of quality. Subsequent to the publication of the scope document, no further information was found or received by EPA that substantiated any of the uses with limited and poor-quality references that had been characterized as "other uses". As a result, these uses were determined to not be intended, known, or reasonably foreseen conditions of use. This list included the following: Applications in odor agents, cleaning/washing agents, surface treatment, absorbents and adsorbents, laboratory chemicals, light-harvesting materials, transistors, molecular switches, solar cells, optoelectronic devices, paper, architectural uses, polyester fibers, adhesion, motors, generators, vehicle components, sporting goods, appliances, agricultural equipment and oil and gas pipelines (EPA-HQ-OPPT-2016-0725-0004). Furthermore, EPA does not believe that it is appropriate to categorically consider all activities that occurred in the past but are not currently occurring to constitute reasonably

	• EPA refused to analyze certain exposure pathways in depth. (13_262) • EPA should not dismiss exposure pathways on a cursory basis and must consider those exposures when evaluating the combined exposures, not make unjustified exclusions and cursory analyses (13_264, 13_266). • When EPA declines to analyze an exposure pathway further, EPA must have a sound, rational basis for the assessment of that exposure and consider how it may combine with other exposure sources (13_263).	foreseen conditions of use. As explained in the *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* rule preamble, 82 FR 33726, 33730-1 (July 20, 2017), "[i]t is reasonable to foresee a condition of use, for example, where facts suggest the activity is not only possible but, over time under proper conditions, probable." EPA considered all potential routes of exposure. Based on the physical chemical properties of PV29 and available data about the potential hazards and exposures of PV29, EPA determined that inhalation exposure from manufacturing and processing is the primary route of concern, so this route of exposure was assessed quantitatively. EPA included a screening level assessment of risks to workers as a result of inhalation exposures in the final Risk Evaluation. EPA determined that oral exposure was not a relevant route of exposure, as eating, drinking and smoking are prohibited in the PV29 production facility, with the low hazard reported in all oral toxicity studies and the low potential for absorption meant that no risk concerns were identified from oral exposure for all conditions of use. All occupational uses and exposures have been included and evaluated (Refer to Section 2.3.1). Uncertainties were identified regarding reasonably available information characterizing PV29's occupational worker inhalation exposure. These uncertainties resulted in EPA requiring testing of PV29 to develop new information in order for EPA to increase certainty in the final Risk Evaluation of PV29 under TSCA section 6(b). Test data has been reviewed for data quality according to the relevant data quality evaluation metrics and incorporated into the final Risk Evaluation. Since that data collected was in direct response to comments on the draft risk evaluation, EPA has determined that it is not warranted for this risk evaluation to be reissued for public comment.

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		EPA does not lack information – EPA has used reasonably available information and used test order authority where there were uncertainties. Refer to section 2.3.1 in the risk evaluation for the occupational exposures for the conditions of use. EPA has not excluded any condition of use for this evaluation. Each condition of use is intended, known, or reasonably foreseen. The only identified consumer condition of use of PV29 was use in artistic paints and watercolors (Section 3.3.2). Exposures from this condition of use are expected to be low based on physical chemical properties and/or well below those exposures likely to occur compared to occupational users. There were no uses determined to be reasonably foreseeable. As described in a preceding response, there were a group of "other uses" that were identified early in the process with poor quality references. Subsequent to the publication of the scope document, no further information was found or received by EPA that substantiated any of the uses with limited and poor-quality references that had been characterized as "other uses". As a result, these uses were determined to not be intended, known, or reasonably foreseen and are not conditions of use. PV29 as an intermediate is included as a condition of use. Once PV29 is used as an intermediate, it is no longer present; therefore, end products formed following reactions using PV29 as an intermediate are not conditions of use of PV29 and thus are not evaluated. General population and consumer exposures were evaluated to the degree possible given the reasonably available data and expected routes of exposure.

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		There is low confidence in the result of aggregating exposures and risks for this chemical if EPA uses an additive approach due to the uncertainty of the data. EPA does not have data that could be reliably modeled for the aggregate exposure.
EPA failed to consider workers experiencing multiple routes of exposure		
8, 12, 13	• EPA failed to account for multiple routes of occupational exposure, such as cleaning paint booths and other locations. (13_8, 13_211, 12_9) • EPA's "screening-level analysis of sentinel exposure (dermal and inhalation) to workers" is inadequate because it fails to mention the potential that a worker might be exposure by both inhalation and dermal routes. (13_197) • EPA repeatedly understates the risks to exposed workers when calculating dermal and inhalation exposures by ignoring the fact that many workers will face both; EPA does not evaluate whether PV29 is safe for workers who both touch and inhale it. (12_16) • EPA's series of rationales for dismissing the significance of worker exposures are weak and based on little actual data or analysis. (13_161) • EPA was unclear in its assumptions regarding dermal exposure levels (8_12)	TSCA section 6(b)(4)(F)(ii) directs EPA to "describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration" in risk evaluations. There is low confidence in the result of aggregating the dermal and inhalation risks for this chemical if EPA uses an additive approach, due to the uncertainty in the data. EPA does not have data that could be reliably modeled into the aggregate, which would be a more accurate approach than adding, such as through a PBPK model. Using an additive approach to aggregate risk in this case would result in an overestimate of risk. Given all the limitations that exist with the data, EPA's approach is the best available approach. EPA has updated its assumptions regarding dermal exposure levels in the final Risk Evaluation.
Deficiencies in exposure data and analysis		
8, 13, 16, 18, 75	<u>PUBLIC COMMENTS:</u> • EPA lacks critical exposure information for PV29 and took no steps to require the submission or development of any more exposure data. As a	TSCA requires EPA to use reasonably available information and best available science in its risk evaluation. Utilizing the systematic review process, EPA used reasonably available data and best available science in a weight of scientific evidence analysis. EPA identified uncertainties regarding reasonably available information characterizing the solubility and occupational inhalation exposure (including duration,

	result, the evaluation has major exposure data deficiencies (13_80). • EPA lacks substantial evidence on occupational exposures from the inhalation and dermal routes. (13_90) • EPA did not comply with TSCA because it did not consider the likely duration, intensity, frequency, or number of exposures for PV29 (13_187, 13_310). • EPA should require the following data: (13_284) Use data – Range of concentrations in industrial, commercial, and consumer products – Measured levels of residual PV29 left in products made using PV29 as an intermediate, where PV29 is a reactant or where PV29 is added to adjust the color of other pigments – Empirical data on frequency of product use for industrial, commercial, and consumer products – Empirical data on duration of product use for industrial, commercial, and consumer products Fate data – Measured data on absorption by inhalation, dermal, and oral routes, for PV29: – as produced in solid (powder) form – as produced in solution form – in each type of formulation in which it is present – Measured water solubility in a reliable study that accurately accounts for pH – Measured bioconcentration factor (BCF) and bioaccumulation factor (BAF) – Appropriate values to assess bioconcentration/bioaccumulation directly from air Environmental release and exposure data	intensity, frequency, or number of exposures for PV29) for PV29. These uncertainties resulted in EPA requiring testing of PV29 to develop new information, in order for EPA to increase certainty in the final Risk Evaluation of PV29 under TSCA section 6(b). Test data has been received, reviewed for data quality according to the relevant data quality evaluation metrics and incorporated into the final Risk Evaluation. For all data elements, except when it relates to solubility or inhalation exposure, EPA determined that it has sufficient reasonably available information. With the generation and submission of the additional testing under TSCA section 4, EPA now has sufficient reasonably available information for all data elements relevant to PV29. Where assumptions were used in the final Risk Evaluation as a result of deficiencies in the available data, these were explained clearly in the final Risk Evaluation. Where EPA received additional data from the manufacturing stakeholders of PV29 to reduce uncertainties about the manufacturing practices and environmental releases of PV29, in the form of. correspondences with manufacturing stakeholders, this was made publicly available in the docket in the *Supplemental File: Information Received from Manufacturing Stakeholders* U.S. EPA (2020a). This information includes SDSs as well as updates to the Environmental release information (described in Section 3.2) New occupational exposure estimates were added for the manufacturing workers. These estimates were prepared using recent monitoring data and several conservative assumptions. The new screening level occupational exposure for the down-stream processors and users were added. These estimates use several conservative assumptions which will cover the worst-case scenarios.

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	– Measured data for air, water, and waste releases from sites of manufacture, processing, and industrial or commercial use; wastewater treatment (both effluent and sludges/biosolids); landfill leachate and effluent and sludges/biosolids from leachate treatment – Measured data for presence/concentration in environmental media and organisms (air, water, sediment; aquatic, sediment-dwelling, and terrestrial organisms) near manufacturing, downstream processing and use, and disposal and land (biosolids) application sites – Occupational exposure data (for all manufacturing and downstream processing and use sites) – Monitoring of air concentrations, for dust, mists, aerosols, vapors (75_2) – Monitoring of dust on surfaces and concentrations in solutions in all settings where skin contact with the surfaces or solutions could potentially occur – Numbers of workers potentially exposed in each activity/setting, at each site – Specific engineering controls, PPE and workplace practices in place at each site/setting, and data on their extent of use and efficacy – SDSs: If EPA plans to rely on SDSs, then EPA needs empirical data on extent of their availability and comprehension to all potentially exposed workers; their completeness, accuracy and currency; extent of compliance with protective measures they specify	
Opposition to EPA's reliance on personal communication from Sun Chemical		

#	Summary of Comments for Specific Issues Related to Charge Question 4	EPA/OPPT Response
9, 10, 12, 13, 15, 18	PUBLIC COMMENTS: • EPA should not have relied on the single personal communication with Sun Chemical Corporation to obtain "air monitoring data" and the "maximum air concentration value." (9_11, 10_5, 12_12, 13_86, 13_93, 15_9, 18_8) Sun Chemical Corporation is an entity with a strong interest in having EPA find its chemical safe. (13_93) • By relying on this personal communication with the potentially regulated manufacturer, EPA failed to include the full range of job tasks, chronic health/exposure studies, and representative monitoring data necessary to evaluate occupational exposure. (18_8) • While EPA uses this value, the Agency knows nothing about the data quality, how the concentration was determined, or what this workplace air value actually represents. This personal communication does not constitute the "best available science." (9_11, 12_12, 15_9, 10_5) • OSHA refuses to rely on undocumented exposure measurements offered by industry without study details and requires employers to preserve exposure records; EPA should have requested these monitoring data and protocols from employers (*i.e.*, Sun Chemical Corporation) in order to evaluate their data submission. (12_14) • EPA should take steps to allow workers to provide input in a manner that reduces the risks of any potential retaliation from management. (13_297)	EPA acknowledges the uncertainty related to the use of a point estimate to describe potential workplace exposure to PV29 dust as a result of workplace activities. In response to these uncertainties as well as public and SACC comments, EPA issued a TSCA Section 4(a)(2) Test Order for PV29 on February 28, 2020. This Test Order required the generation and submission of a workplace air monitoring study of particles not otherwise regulated, conducted according to the NIOSH 0600 guideline available at: https://www.cdc.gov/NIOSH/DOCS/2003-154/pdfs/0600.pdf. This study takes into account a full range of job tasks and representative monitoring of actual PV29 production at the sole U.S. manufacturing facility of PV29. This study has been evaluated for data quality and the results are incorporated into the final Risk Evaluation for PV29. More information about the Section 4 Test Order for PV29 can be found in the docket (EPA-HQ-OPPT-2020-0070-0008). During the data collection phase of the Risk Evaluation process, EPA welcomed comments and information on occupational exposure. The Agency did not receive any comments considered.
Concern regarding EPA's approach to evaluate only highest anticipated exposure		

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13	PUBLIC COMMENTS: • EPA's assertion that it need only account for the highest anticipated exposure ignores the potential that multiple sources of exposure (*e.g.*, at work and at home) may engender a risk greater than the risk from the highest exposure alone. (13_196, 13_198) • EPA's decision to conduct only a screening-level assessment of certain workers and claim that it can serve as the sole sentinel exposure for all other human exposures is scientifically corrupt and fails to meet TSCA's mandates. (13_200)	TSCA section 6(b)(4)(F)(ii) directs EPA to "describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration" in risk evaluations. EPA defines aggregate exposures as the combined exposures to an individual from a single chemical substance across multiple routes (*i.e.*, dermal, inhalation, or oral) and across multiple pathways (*i.e.*, exposure from different sources). 40 CFR 702.33. EPA defines sentinel exposures as the exposure from a single chemical substance that represents the plausible upper bound of exposure relative to all other exposures within a broad category of similar or related exposures. 40 CFR 702.33. EPA considered the reasonably available information and used the best available science to determine whether to consider aggregate or sentinel exposures for a particular chemical. EPA has determined that using the high-end risk estimate for inhalation risks separately from other pathways as the basis for the unreasonable risk determination is a best available science approach. There is low confidence in the result of aggregating the risks from various exposure pathways for this chemical if EPA uses an additive approach, due to the uncertainty in the data. EPA does not have data that could be reliably modeled into the aggregate, which would be a more accurate approach than adding, such as through a PBPK model. Using an additive approach to aggregate risk in this case would result in an overestimate of risk. Given all the limitations that exist with the available data, EPA's approach is the best available science. Available data for PV29 indicate low hazard and low potential for exposures. As a result, it was determined that a mix of quantitative assessment and qualitative, screening-level assessment, was the most optimal approach to focus

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		efforts on the exposure pathways that are most likely to result in potential risks.
Supports tiered approach that incorporates PPE in the exposure assessment		
17	PUBLIC COMMENTS: • EPA should use a tiered approach to exposure assessment that incorporates PPE. Margin of exposure (MOE) calculations did not account for PPE (which is acceptable in this case), but EPA should use higher tier methods that account for worker protections when necessary. (17_19)	In the final Risk evaluation, EPA calculated risks to workers without PPE and with PPE.
Opposes assumption of PPE use in the exposure assessment		
11, 12, 13, 15, 16, 18, 44, 77, 82	PUBLIC COMMENTS: • EPA should not use the baseline assumption that PPE is used, and used correctly, when assessing occupational exposure. (18_12, 13_166, 12_18, 15_2) • EPA makes incorrect assumptions regarding absence of data, extrapolation of data to alternate exposure routes, exposure characteristics, use of PPE, adherence/enforcement to workplace policies (*i.e.*, no-eating-or-smoking policy), model inputs, and similarities between PV29 and other chemicals. (11_6, 12_18, 13_7, 13 _98, 13_99, 13_101, 13_103, 13_167, 15_2; 16_37, 16_94, 18_11, 44_5, 77_4, 82_3) • There appear to be no empirical data to document the extent of use or effectiveness of any of	Through correspondences with Sun Chemical, and by consulting the SDSs available for PV29, EPA has gathered information about the types of PPE utilized throughout the manufacturing process for PV29. This information is being made publicly available in the *Supplemental File: Information Received from Manufacturing Stakeholders* U.S. EPA (2020a). Statements on SDS and use of PPE used by the downstream processors and users were updated to indicate the uncertainties. For the purpose of this Risk Evaluation, EPA makes assumptions about potential PPE use based on reasonably available information and expert judgment. EPA considers each condition of use and constructs exposure scenarios with and without engineering controls and /or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal

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	industrial hygiene controls, such as PPE or SDS adherence. (13_169) • EPA should use its authority to require data in order to have empirical data on actual use of PPE. (13_284) • No information is provided on the type of PPE used and whether it is sufficiently protective to reduce oral exposure. (13_168) • Given that EPA has not identified the workplaces where PV29 is used, it has no basis for assuming the use or effectiveness of unspecified PPE. (12_18) • EPA has an obligation to evaluate exposures and risks for the subset of people for whom engineering controls are not in place or do not reach 100% efficiency. (13_302)	regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in Section 5. Additionally, in consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in Section 5 and EPA's assumptions are described in the unreasonable risk determination for each condition of use. In the case of PV29, risks were not identified for oral exposure because of low exposure and low hazard for oral exposure. Therefore, use of workplace practices prohibiting eating, drinking and smoking in manufacturing and processing facilities is important but not an ultimate determining factor in whether risks are expected for oral exposure.
EPA should not rely on the presence of and compliance with safety data sheets (SDS)		
11, 12, 13, 15, 18	PUBLIC COMMENTS: • It is unacceptable for EPA to rely on the presence of accurate, well-understood SDSs and that workers and employers will comply with SDSs as a means to minimize occupational exposure. (18_13, 13_166, 11_7, 15_14) • EPA provides no evidence to support this assumption that workers will read and understand	Statements on PPE use by the downstream processors and users were updated to include a discussion of the uncertainties. As stated above, for the purpose of this Risk Evaluation, EPA makes assumptions about potential PPE use based on reasonably available information and expert judgment. EPA considers each condition of use and constructs exposure scenarios with and without engineering controls and /or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has

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	SDS; in fact, there is extensive evidence it is incorrect in many instances. (11_7) • SDSs should not be a substitute for a workplace control plan to eliminate and mitigate PV29 occupational exposure. (18_13) • EPA assumes without evidence that engineering controls and PPE described in unpublished industry SDSs are universally used in all workplaces. (13_172) • Manufacturer admonitions on SDSs are not enforceable and cannot support a determination that PV29 presents no unreasonable risk. (12_18) • Workers and small employers often have a great deal of trouble understanding SDSs. Employers often ignore not only SDS recommendations, but basic, common-sense safety rules. (11_11) • SDSs often contain inaccuracies and are incomplete, as concluded by a review study of 24 SDSs. (11_13) • EPA appears to be operating under a significant misunderstanding of OSHA's Hazard Communication Standard (HCS); a recommendation on a safety data sheet by itself would not trigger the need to implement new controls. (11_8, 11_9)	evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in Section 5. Additionally, in consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. The OSHA regulations at 29 CFR 1910.132 require employers to assess a workplace to determine if hazards are present or likely to be present which necessitate the use of personal protective equipment (PPE). If the employer determines hazards are present or likely to be present, the employer must select the types of PPE that will protect against the identified hazards, require employees to use that PPE, communicate the selection decisions to each affected employee, and select PPE that properly fits each affected employee.
EPA should prioritize engineering controls over PPE or warning labels to reduce exposure		
11, 12, 13, 15, 18	PUBLIC COMMENTS: • Under OSHA Hierarchy of Controls, PPE is the least effective form of protection; EPA should use this hierarchy and prioritize measures to reduce occupational exposure, not rely on PPE or warning	As indicated above, for the purpose of this Risk Evaluation, EPA makes assumptions about potential PPE use based on reasonably available information and expert judgment. EPA considers each condition of use and constructs exposure scenarios with and without engineering controls and /or PPE

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	labels to reduce exposure (18_14, 13_307, 15_16, 12_19) • There is widespread support, including in court, for the hierarchy of control. (18_15) • The most effective way to control dust in the workplace is through engineering controls, rather than PPE; reliance on PPE rather than engineering controls is unacceptable. (11_4)	that may be applicable to particular worker tasks on a case-specific basis for a given chemical.
Concerns about lack of release data		
13	PUBLIC COMMENTS: • EPA has no actual data on the levels of PV29 released to or present in workplaces, products, or environmental media and has not used its authorities to require these data. (13_84)	EPA requested additional info detailing possible releases of PV29 to the environment. That information is communicated in Section 3.2 and the *Supplemental File: Information Received from Manufacturing Stakeholders* with resultant releases to surface water being <1lb/day U.S. EPA (2020a). Other PV29 that may be captured in wastewater sludge is disposed of via permitted landfills
Support for EPA's engagement with industry to obtain data		
19	PUBLIC COMMENTS: • EPA did the right thing by engaging with industry and seeking actual data to answer its questions, *i.e.*, for working with Sun Chemical to understand the manufacturing conditions and potential for worker exposures and environmental releases. (19_14)	EPA acknowledges the comment and has made no change.
Concerns about occupational inhalation exposure assessment assumptions and parameters		
13, 78	PUBLIC COMMENTS: • EPA calculated a potential dose rate based on a NIOSH inhalation exposure rate that is over 40 years old, which is inadequate, or EPA should provide empirical evidence supporting its use. (13_8, 13_202) • EPA assumes without explanation or justification that workers could inhale PV29 only in dust form.	EPA has updated the risk evaluation to incorporate actual monitoring information collected from the sole US manufacturer of PV29, Sun Chemical. Through communications with Sun Chemical, EPA obtained information that Sun Chemical utilized the exposure limit for respirable dust and conducted monitoring data to ensure that that the amount of respirable dust in the manufacturing facility was below this level. This information along with all

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	CPMA submitted a comment noting use of PV29 in downstream applications involving high heat (could generate vapors) or spraying (could generate mists or aerosols), yet EPA fails to mention or analyze the potential for inhalation of forms other than powder or dust. (13_95, 13_97) • EPA should clarify the procedure through which PV29's particle size distribution was calculated, and, if bulk material was tested, redo its analysis to reflect the size distribution for the airborne particles to which workers are exposed. (78_10)	information used in the assessment that was provided by the US manufacturing stakeholders for PV29 can be found in the *Supplemental File: Information Received from Manufacturing Stakeholders* U.S. EPA (2020a). Workers may be exposed to mist (paint and ink) Downstream exposure estimate using OSHA PEL is applicable for mist exposure and a statement on possible mist exposures for the relevant conditions of uses was included. Particle size distribution data is available in the *Supplemental File: Information Received from Manufacturing Stakeholders* U.S. EPA (2020a).
Concerns about occupational dermal exposure analysis and clarity		
13	PUBLIC COMMENTS: • To assess dermal occupational exposure, EPA relied on modeling, even though EPA itself acknowledges that measured workplace exposure data is preferable to modeling. (13_91) • Some aspects of the modeling are conservative (*e.g.*, a "high" default for the amount of solid material contacting skin, assumed no use of gloves) and others are not (*e.g.*, assumed single exposure event per worker per day, assumed a single worker is exposed per day) even though the range of activities to which the model applies would clearly have the potential to involve multiple exposures per day or exposure of multiple workers. (13_99) • EPA presented only a single dermal exposure scenario that it claims represents the "theoretical	Input parameters and assumption for the inhalation and exposure modeling are consistent with those used in other OPPT assessments including the TSCA New Chemicals program.

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	maximum exposure" with no basis for this characterization. (13_99) • EPA's dermal exposure analysis assumed only PV29 in solid form, yet PV29 is also produced in the form of a high-concentration solution. (13_6, 13_96, 13_101) • EPA hand-waves away dermal exposure in part by assuming that PPE is always used and used effectively. (13_182)	
EPA should revisit its decision not to assess occupational oral exposure		
12, 13, 15	PUBLIC COMMENTS: • EPA's argument assumes that oral exposure only occurs if workers eat contaminated food or smoke is incorrect. (13_167) • This argument assumes without any documentation that there is 100% compliance with the no-eating-or-smoking policy. Research has revealed that incidental ingestion from hand-to-mouth contact occurs in the workplace. (13_167) • EPA should more closely assess the potential for oral exposure via pathways beyond ingestion of contaminated food. (13_168) • Dermal and inhalation exposures make oral ingestion likely in a workplace. (12_16) • EPA hand-waves away oral exposure in part by assuming that PPE is always used and used effectively. (13_182, 12_18) • EPA's blanket rejection of the oral route of exposure is not supported by science; it has been estimated that approximately one in six workers may be involved in tasks in which inadvertent ingestion exposure could contribute to their total body burden. (15_14)	EPA agrees that oral exposures are possible other than from contaminated food or smoking. EPA's inhalation exposure estimate included oral exposure via incidental ingestion of inhaled mist/dust. However, EPA currently does not have data or methods to fractionate the total PV29 inhaled into the amount of PV29 that deposits in the upper respiratory system and the amount of PV29 that goes into the lung. EPA generally does not separately evaluate occupational exposures through the oral route. Workers may inadvertently transfer chemicals from their hands to their mouths or ingest inhaled particles that deposit in the upper respiratory tract. The frequency and significance of this exposure route are dependent on several factors including the physical-chemical properties of the substance during worker activities, the visibility of the chemicals on the hands while working, workplace training and practices, and personal hygiene that is difficult to predict Cherrie et al. (2006). EPA may consider the relevance of oral exposure route on a case-by-case basis, taking into consideration the aforementioned factors and any reasonably available information, and may assess oral exposure for workers for certain COUs and worker activities where warranted. For

#	Summary of Comments for Specific Issues Related to Charge Question 4	EPA/OPPT Response
		PV29, EPA did not find any information indicating significant oral exposure during the systematic review of the materials found.
EPA did not properly assess exposure of downstream processors and users		
11, 12 13, 15, 16, 44, 55	PUBLIC COMMENTS: • EPA assumes that downstream processors and users are at low risk of exposures because they wear PPE, which is an incorrect way to assess health risk. (13_11, 15_21) • EPA restricts its occupational exposure analysis to the site of manufacture, failing to account for worker exposures at downstream processing and use sites. (13_154) • EPA does not appear to have received or obtained significant information from the processors of PV29, only the sole manufacturer. (13_288) • EPA's analysis is based on the unsupported assertion that downstream worker exposure and industrial uses will be less than manufacturing exposure because volume handled is less and the manufacturing exposure represents a "worst case"; there is no basis for this. (13_6, 11_16, 15_19, 16_7) • It is inappropriate for EPA to discount exposure at processing and use sites since EPA has no data on the of use or efficacy of engineering controls, SDS, and PPE downstream. (13_156) • EPA inappropriately used the approximate maximum workplace air concentration reported in a personal communication from Sun Chemical to	The new screening level occupational exposure for the down-stream processors and users were added. These estimates use several conservative assumptions which will cover the worst-case scenarios. Statements on SDS and PPE use by the down-stream processors and users were updated to indicate the uncertainties.

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	estimate downstream worker exposure. (12_13, 44_11-13, 55_5-6, 55_18, 15_9, 16_7) • Downstream occupational exposure may significantly exceed manufacturing site exposure given the potentially different activities and controls that might be in place. (11_16, 13_107) • EPA has failed to use the best available science for downstream exposure. (13_161, 15_19) • EPA lacks data on potential exposure of downstream workers at processing and use sites, number of sites involved, and number of potentially exposed workers. (13_104) • Without evaluating downstream exposures, PA has no basis for comparing risks faced by manufacturing workers to those who work with or use downstream products. (12_10, 13_187) • EPA has failed to use its authority to collect data on downstream exposure. (13_284)	
Concerns about the environmental release characterization		
13, 16	PUBLIC COMMENTS: • EPA fails to include basic information about environmental release critical for a meaningful assessment of PV29's risks to the environment, as required by TSCA. (16_32) • No calculation or data are presented to support the conclusion that approximately 1-2% of the production volume is released into the environment. (16_46) • EPA relies on industry determination that use is restricted to a single site; as a result, sources of exposure are overlooked. (13_77, 13_78) • The only remotely "quantitative" element regarding exposures is the manufacturer's asserted	EPA requested additional info detailing possible releases of PV29 to the environment and based its environmental risk characterization on the best reasonably available information. The information received from communications with Sun Chemical is communicated in Section 3.2 and 2 and the *Supplemental File: Information Received from Manufacturing Stakeholders* with resultant releases to surface water being <1lb/day U.S. EPA (2020a). Other PV29 that may be captured in wastewater sludge is disposed of via permitted landfills. EPA concedes the uncertainty associated with this information and has added language discussing this uncertainty. Nevertheless, it was the best reasonably available information concerning possible releases of PV29 to the

	estimate for water discharges from its facility, but this value is unreliable and insufficient. (13_188) • EPA does not properly analyze distribution and gives no attention to potential releases and exposures resulting from accidental releases. (13_268, 13_269) • EPA's analysis of biosolids is particularly lacking; a thorough analysis of biosolids would be appropriate given that PV29 is poorly biodegradable. (13_266)	environment and felt it was worth including due to the absence of other information. Accidental releases Spills and leaks generally are not included within the scope of a TSCA risk evaluation. EPA is exercising its authority under TSCA to tailor the scope of the risk evaluation for PV29, rather than evaluating activities which are determined not to be circumstances under which PV29 is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, or environmental exposure pathways addressed by another EPA-administered statute and associated regulatory program. First, EPA does not identify PV29 spills or leaks as "conditions of use." EPA does not consider PV29 spills or leaks to constitute circumstances under which PV29 is manufactured, processed, distributed, used, or disposed of, within TSCA's definition of "conditions of use." Congress specifically listed discrete, routine chemical lifecycle stages within the statutory definition of "conditions of use" and EPA does not believe it is reasonable to interpret "circumstances" under which MC is manufactured, processed, distributed, used, or disposed of to include uncommon and unconfined spills or leaks for purposes of the statutory definition. Further, EPA does not generally consider spills and leaks to constitute "disposal" of a chemical for purposes of identifying a COU in the conduct of a risk evaluation. In addition, even if spills or leaks of PV29 could be considered part of the listed lifecycle stages of PV29, EPA has "determined" that spills and leaks are not circumstances under which MC is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, as provided by TSCA's definition of "conditions of use," and EPA is exercising its discretionary authority to exclude MC spills and leaks from the scope of the MC risk evaluation. The exercise of that authority is informed by

		EPA's expertise in developing scoping documents and risk evaluations, and on various TSCA provisions indicating the intent for EPA to have some discretion on how best to address the demands associated with implementation of the full TSCA risk evaluation process. Specifically, since the publication of the Risk Evaluation Rule, EPA has gained expertise by conducting ten risk evaluations and designating forty chemical substances as low- and high-priority substances. These processes have required EPA to determine whether the case-specific facts and the reasonably available information justify identifying a particular activity as a "condition of use." With the experience EPA has gained, it is better situated to discern circumstances that are appropriately considered to be outside the bounds of "circumstances… under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of" and to thereby meaningfully limit circumstances subject to evaluation. Because of the expansive and potentially boundless impacts that could result from including spills and leaks as part of the risk evaluation, which could make the conduct of the risk evaluation untenable within the applicable deadlines, spills and leaks are determined not to be circumstances under which PV29 is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, as provided by TSCA's definition of "conditions of use." Exercising the discretion to not identify spills and leaks of PV29 as a COU is consistent with the discretion Congress provided in a variety of provisions to manage the challenges presented in implementing TSCA risk evaluation. See *e.g.*, TSCA sections 3(4), 3(12), 6(b)(4)(D), 6(b)(4)(F). In particular, TSCA section 6(b)(4)(F)(iv) instructs EPA to factor into TSCA risk evaluations "the likely duration, intensity, frequency, and number of exposures under the conditions of use…," suggesting that activities for which duration, intensity, frequency, and number of exposures

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		cannot be accurately predicted or calculated based on reasonably available information, including spills and leaks, were not intended to be the focus of TSCA risk evaluations. And, as noted in the preamble to the Risk Evaluation Rule, EPA believes that Congress intended there to be some reasonable limitation on TSCA risk evaluations, expressly indicated by the direction in TSCA section 2(c) to "carry out [TSCA] in a reasonable and prudent manner." EPA qualitatively assessed discharges of PV29 in biosolids based on its physical chemical and fate properties. Based on its low solubility (<0.003 mg/L), PV29 in land-applied biosolids is not expected to leach to soil or groundwater. PV29 is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs.
EPA did not consider environmental release of PV29 when used as an intermediate		
13	PUBLIC COMMENTS: • EPA asserts without evidence that use of PV29 as an intermediate does not result in environmental releases and exposures and does not mention the potential for PV29 to remain in products generated from its use as an intermediate. (13_71) • EPA leaves open the question of whether intermediate use of PV29 is restricted to a single site or may involve more than one site, which would involve storage, transport, and transfer and thus greater risk of release and exposure. (13_76)	EPA does not have information one the residual PV 29 after it is used as a chemical intermediate for the manufacture of other pigments. However, release and exposure from any residual PV29 is expected to be lower than the exposure and releases from use of PV29.
Concern about assumption that PV29 remains "bound" in downstream use		

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13, 16(S)	PUBLIC COMMENTS: • There are reasons to question the notion that PV29 is "bound in a matrix" once in consumer products, including at end-of-life. (16(S)_9) • EPA failed to consider the disposition of PV29 when products, including plastics, enter the waste and recycling streams, where any "encapsulated" compound may be released. (16(S)_11) • EPA should not rely on a food additives petition to FDA that is not publicly available to conclude that PV29 will not leach from plastics or paints. (13_171)	As stated in the risk evaluation, PV29 is not expected to leach out of plastics when it is encapsulated. PV29 demonstrates negligible solubility in both octanol and water, and no toxicity effects were observed following oral or dermal exposure. Additional data, submitted to fulfil the conditions of the Section 4 test order confirm that PV29 exhibits a low solubility in octanol and water (<0.003 mg/L). This reduces the uncertainties about whether PV29 would be expected to leach from plastics once it is encapsulated. Furthermore, risks were not identified at the highest exposure concentrations during manufacturing, so risks are not expected to result from exposure to PV29 in plastics, as these potential exposures are negligible. EPA is not relying on the results of the food additive petition to draw conclusions about the potential for PV29 to leach from plastics. The same data are used in this assessment as well as in the food additive petition and as a result, similar conclusions were drawn in both documents regarding the potential for leaching from plastics.
EPA was right to remove conditions of use it was unable to support		
8, 17, 45	• EPA was right to remove "other uses" and "import" as conditions of use due to the inability to support these uses. If there were no data of concern or all uses were already covered and non-standard uses were not anticipated, EPA should make such a statement. (8_7, 17_5, 45_3)	Based on information provided in public comments, EPA has included import as a condition of use of the evaluation (see section 1.5 of the final Risk Evaluation).
Evaluation lacks information on conditions of use		
12, 13, 16, 16(S), 82	PUBLIC COMMENTS: • The draft risk evaluation lacks crucial information on the conditions of use of PV29. In particular, EPA ignored the presence of PV29 in products made using PV29 as an intermediate even though	Intermediates are evaluated in the risk evaluation. EPA prepared exposure estimates using OSHA PEL for total and respirable dust which results in a protective approach and

	the evidence in the record establishes that PV29 often remains present in such products. (13_5) • EPA has provided no analysis explaining why "import" and the "other" uses are no longer considered reasonably foreseen, especially given that PV29 has a domestic market and is sold to downstream processors and users, so may be imported in the future. It is reasonably foreseeable that persons might use PV29 in those same circumstances in the United States if persons already use PV29 for those purposes abroad. (13_63 & 66) • EPA made no effort to further identify "unknown" uses. (16_41) • By dismissing certain conditions of use based on little evidence, EPA violates its duty under the statutory language to consider all conditions of use, exposures, and hazards. (13_244) • By excluding downstream conditions of use (*e.g.*, candles, carpet fibers, paint, coatings), EPA failed to evaluate downstream worker and consumer exposure. (12_9, 16(S)_8) • The risks of these additional activities, in combination with those from the originally intended activities, could well increase to a point where EPA would find that the chemical "presents" or "may present" an unreasonable risk. Hence it is vital that EPA consider both intended and reasonably foreseen conditions of use in its initial review. (82_4)	represents all downstream processors and users who might be exposed to dust or mist containing PV29 in products. Following the publication of the Draft Risk Evaluation, information was received from a group of NGOs indicating that BASF Corporation imports C.I. Pigment Violet 29 in volumes less than 25,000 pounds per year (EPA-HQ-OPPT-2018-0604-0016). Therefore, import of C.I. Pigment Violet 29 is included as a condition of use. A list of "other uses" was compiled during EPA's initial search for PV29 conditions of use. This list of other uses included the following: Applications in odor agents, cleaning/washing agents, surface treatment, absorbents and adsorbents, laboratory chemicals, light-harvesting materials, transistors, molecular switches, solar cells, optoelectronic devices, paper, architectural uses, polyester fibers, adhesion, motors, generators, vehicle components, sporting goods, appliances, agricultural equipment and oil and gas pipelines (EPA-HQ-OPPT-2016-0725-0004). However, no further evidence was found or submitted during the scope, problem formulation and draft risk evaluation steps to support these "other uses" as intended, known, or reasonably foreseen conditions of use for C.I. Pigment Violet 29. As a result, these uses were determined to not be intended, known, or reasonably foreseen conditions of use. EPA disagrees that it made no effort to further identify unknown uses or dismissed certain conditions of use based on little evidence. EPA conducted extensive research and outreach including review of published literature and online databases including the most recent data available from EPA's Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of C.I. Pigment Violet 29 and queried government and commercial trade databases. EPA also received comments on the *Scope of*

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		the Risk Evaluation for Pigment Violet 29 (U.S. EPA, 2017c) that were used to determine the current conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities and a September 15, 2017 meeting with several representatives from trade associations. In any event, EPA disagrees that it has a statutory duty to consider all conditional of use in each risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider" in a risk evaluation, suggesting that EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis. (82 FR 33736, 33729; July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimis exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or use as an intermediate) or that have been adequately assessed by another regulatory agency. EPA has included a more detailed discussion of potential risks to downstream conditions of use in the final Risk Evaluation. EPA plans to consider all reasonably foreseen uses as they apply to PV29.
Inadequate characterization of potentially exposed or susceptible sub-populations (PESS)		

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11, 13, 14, 16	PUBLIC COMMENTS: • EPA dismissed concerns about exposures of vulnerable subpopulations, distorting the law's definition and failing to meet TSCA's requirements. (13_190, 16_37) • EPA's approach of accounting for the highest anticipated exposure ignores the potential that a lower exposure may result in greater risk to a member of a vulnerable subpopulation. (13_196, 14_14) • EPA should identify people living near disposal sites, sources of contamination, and other conditions of use as PESS. (13_298) • EPA should always evaluate exposures scenarios without engineering controls and PPE in order to assess exposures and risks to those subpopulations not subject to such controls. (13_301) • Workers are a relevant PESS, and EPA has not provided adequate evidence that it has made an accurate determination as required by TSCA. (11_17) • EPA assertions that the risk evaluation is protective of workers, consumers and the general population are not supported by data. (14_20)	EPA uses the high-end exposure value when making its unreasonable risk determination in order to address uncertainties around PPE usage as well as to capture exposures for PESS. Because EPA is making its unreasonable risk determinations on the high-end exposure value for workers and either the high-end exposure value or central tendency for ONUs, depending on the data, and factoring in the uncertainties due to UF factors, it is unclear how this is a flawed approach. Additionally, EPA makes an unreasonable risk determination and makes no determination on reasonable risk.
Support for and request for clarity regarding quantitative screening-level exposure assessment		
8, 17	PUBLIC COMMENTS: • Two commenters generally support the quantitative screening level exposure assessment approach used by EPA. (17_16, 8_8) • EPA should explain why a quantitative screening-level exposure assessment was added, given that it	EPA initially proposed the screening level-approach in the assessment for human health to incorporate available data to create a high-end risk estimate for the most highly exposed subpopulation, which was determined to be workers at the sole US manufacturing facility of PV29. Where data were not

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	was not anticipated in the problem formulation and scoping phase. (17_16, 8_8) • EPA should explain how quantitative exposure assessment data were obtained and checked for their reliability and accuracy. (8_8)	available, monitoring data received from the manufacturer for respirable dust to represent a worst-case exposure scenario. After problem formulation, EPA chose to perform additional quantitative analysis to increase confidence in the results of its screening-level assessment. In response to comments received from the public as well as the SACC, EPA has worked to obtain additional exposure information for PV29 in order to refine and enhance the conclusions made in the initial screening-level risk calculations.
EPA did not address exposures in pregnant women, children, and other downstream users		
9, 10, 12, 16, 16(S)	PUBLIC COMMENTS: • EPA's evaluation of PESS does not cover populations that are known to be more susceptible to chemical hazards, such as pregnant women or children, particularly workers who could be pregnant. (12_20) • EPA fails to consider downstream exposure of users of products such as paints, art supplies, toys, food packaging, plastics, candles, and carpets containing PV29, which particularly significant because PV29-containing products can be used by pregnant women and children who are more susceptible to environmental hazards. (9_12, 12_8, 12_9, 12_10, 16(S)_6, 16(S)_7, 16(S)_8) • EPA cannot assume that pregnant women or children exposed during downstream use have lesser exposures and are adequately protected. (16_37) • Children crawling on carpets containing PV29 can potentially be exposed through dermal contact and ingestion. PV29 can also become dispersed into the indoor environment through routine abrasion and cleaning. (16_39)	As stated in the risk evaluation, the reasonably available data does not indicate increased susceptibility for any particular group or subpopulation. In addition, based on available data for high end exposure to workers handling PV29 in an occupational setting, EPA is confident that this presents a high-end exposure scenario.

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EPA was correct to focus on sentinel exposure		
17, 19	PUBLIC COMMENTS: • EPA was correct to focus on sentinel exposure for PV29, but if the Agency conducts aggregate exposure assessments in the future, it must be clear about how and what it considered and show that it was appropriate to do so. (17_18) • EPA's conservative assumptions with regard to inhalation and dermal exposures are protective and appropriate. (19_9)	EPA acknowledges these comments and encourages the submitters to consult the final Risk Evaluation for refinements made since the publication of the draft risk evaluation.
Support for aggregate exposure vs. sentinel exposure assessment		
SACC, 10, 13	SACC COMMENTS: • Aggregate exposures should be considered including use of PV29 in food packaging. PUBLIC COMMENTS: • EPA should combine all routes of exposure (including dermal, oral, and inhalation) when making a risk determination. (10_14) • EPA's rationale for adopting a sentinel over aggregate exposure assessment approach is inadequate, distorts the meaning of sentinel exposure assessment, and is not a science-based approach. (13_195)	The presence of PV29 in food packaging is under the purview of the Food and Drug Administration and no information was identified to understand the production and uses of PV29 as a result of these pathways. TSCA section 6(b)(4)(F)(ii) directs EPA to "describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration" in risk evaluations. EPA defines aggregate exposures as the combined exposures to an individual from a single chemical substance across multiple routes (*i.e.*, dermal, inhalation, or oral) and across multiple pathways (*i.e.*, exposure from different sources). 40 CFR 702.33. EPA defines sentinel exposures as the exposure from a single chemical substance that represents the plausible upper bound of exposure relative to all other exposures within a broad category of similar or related exposures. 40 CFR 702.33. EPA considered the reasonably available information and used the best available science to determine whether to consider aggregate or sentinel exposures for a particular chemical. EPA has determined that using the high-end risk estimate for inhalation and risks from other routes of exposure separately as the basis for the unreasonable risk

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		determination is a best available science approach. There is low confidence in the result of aggregating the inhalation risks and other routes of exposure for this chemical if EPA uses an additive approach, due to the uncertainty in the data. EPA does not have data that could be reliably modeled into the aggregate, which would be a more accurate approach than adding, such as through a PBPK model. Using an additive approach to aggregate risk in this case would result in an overestimate of risk. Given all the limitations that exist with the data, EPA's approach is the best available approach.
EPA should pursue exposure and releases information from a wider range of organizations		
SACC	SACC COMMENTS: • More aggressively pursue information from manufacturer(s) of life cycle sustainability assessment (LCSA) targets, purchasers/users of those chemicals, trade associations, and other federal and state regulatory agencies that may have specialized knowledge.	When preparing this Risk Evaluation, EPA obtained and considered reasonably available information, defined in 40 CFR 702.33 as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation. EPA also communicated with manufacturing stakeholders of C.I. Pigment to better understand the production and uses of PV29.
Other SACC comments related to physical chemical properties		
SACC	**SACC COMMENTS:** • Refrain from making sweeping generalizations especially when based on limited and/or uncertain information regarding physical chemical properties or toxicological testing. • Include $J_{max, ss}$ (maximum steady-state dermal flux) estimates in their list of physical chemical properties routinely reported in TSCA risk assessments.	By definition, the maximum steady-state dermal flux is calculated using the dermal permeability coefficient (Kp) and the solubility of a substance both in the same vehicle. Since PV29 is not soluble in any solvents except strong acids, this value cannot be estimated.

Environmental Effects

Charge Question 5.a: Please comment on the evidence used to support the characterization of hazard to ecological receptors from acute and chronic exposure as presented in the document.

Charge Question 5.b: Strong sorption to sediment is indicated as a result of the estimated K_{OC} of 5.0 based on estimations from EPI Suite™. While this indicates that exposures to aquatic organisms in the water column are likely to be low, this also indicates that potential water releases could result in exposure to sediment-dwelling organisms. EPA assumed low hazard to these organisms due to the lack of toxicity observed in the tests conducted with all other aquatic species, particularly *Daphnia magna*. Given the acute hazard profile for this chemical, limited releases, and the physical-chemical characteristics of PV29, please comment on the risk characterization for sediment-dwelling invertebrates.

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Need for more data to evaluate hazard to aquatic ecological receptors		
13, 16, 46	PUBLIC COMMENTS: • There is insufficient data to evaluate potential ecological hazards and risks. EPA has no information on chronic aquatic toxicity or toxicity to sediment-dwelling organisms. (13_7, 13_109-110, 16_101-103, 46_6) • EPA could have required the generation of more ecotoxicity data for PV29 during this risk evaluation, and therefore has failed to consider reasonable available information about ecological hazards. (13_110, 16_104) • EPA bases its conclusion that PV29 presents no environmental hazard solely on acute aquatic toxicity data. According to EPA's Appendix C listings, those studies only examined one endpoint, mortality. (13_140). • EPA should require the following data (13_284) – Acute toxicity to sediment-dwelling organisms – Chronic toxicity including to aquatic organisms including aquatic plants, fish, and aquatic invertebrates	EPA acknowledged the uncertainties regarding the lack of environmental hazard data characterizing the effects of chronic exposure to aquatic organisms and hazard data for sediment-dwelling aquatic organisms. Available environmental hazard data for acute exposure indicated a low hazard and the low solubility and low potential for aquatic releases of PV29 led EPA to conclude that additional environmental hazard data is not a critical data need. To reduce the level of uncertainty in the assessment, EPA included Ecological Structure Activity Relationships (ECOSAR; v.2.0) predictive modeling outputs in the final Risk Evaluation to understand the potential hazards of chronic exposure to PV29 to aquatic organisms. The results of this modeling indicate that environmental hazards following chronic exposure are not expected to result at concentrations below the limit of solubility. This provides an additional indication that hazard data for chronic exposure are not a critical data need. While PV29 is expected to be persistent, it is not expected to bioaccumulate, and additional

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	– Chronic toxicity to terrestrial organisms (including sediment-dwelling organisms) • EPA and Environment Canada relied on acute studies. EPA should not presume that toxic levels will not be reached due to low solubility of PV29. This line of argument cannot rule out that there are chronic effects at lower levels. There is no indication that Environment Canada had any chronic toxicity data for the other pigments. (13_127) • EPA should not assume that data from acute aquatic studies can sufficiently address potential chronic aquatic effects for the same chemical. Many chemicals have been shown to exhibit significantly different acute and chronic toxicity values, and these can differ across species for the same chemical. Among other testing, long-term aquatic toxicity testing is needed for PV29 given its persistence, lack of evidence that it is not bioaccumulative, and concerns from EU member countries that it may be PBT or very persistent and very bioaccumulative (vPvB). (13_111-113, 13_284)	data submitted indicate a low solubility in octanol, further indicating a low bioaccumulation potential. In addition to the discussion above about the critical data needs for chronic ecotoxicity data, EPA disagrees with some of the information presented in the ECHA Community Rolling Action Plan (CoRAP) justification document where PV29 is determined to be a potentially Persistent, Bioaccumulative and Toxic (PBT) substance. The justification document (https://echa.europa.eu/documents/10162/c607549c-1c07-c5d6-d6e2-8d18bff91f3a) categorizes PV29 as a potentially bioaccumulative substance because of uncertainties related to the water solubility, $LogK_{ow,}$ and $LogK_{oa}$ of the chemical substance that stems from discrepancies in the predictive modeling outputs, namely between EpiSuite and ACD/Percepta 14.2.0 predictive models. While EPA does agree that PV29 is a persistent chemical, it determined that water and octanol solubility data were critical data needs in order to finalize the Risk Evaluation. As a result, EPA issued a TSCA Section 4(a)(2) Test Order for C.I. Pigment Violet 29 on February 28, 2020. This test order compelled the creation and submission of solubility data to clarify these uncertainties. These studies concluded that PV29 exhibits an extremely low solubility in both water and octanol (<0.003 mg/L), which led EPA to conclude that $LogK_{ow}$ is not a relevant property for PV29 Nicolaou (2020). In addition, the substance is a solid with a high melting point, so log K_{oa} is not a relevant property for this compound. As indicated above in the "Physical Chemical Properties and Environmental Fate" section, EPA has clarified these uncertainties and does not consider PV29 a PBT substance.
Do not ignore Topkat-predicted acute LC50 for fathead minnow		

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13	• EDF located Environment Canada's specific categorization results for PV29. Those results reveal that the pivotal value Environment Canada used for predicted acute toxicity of PV29 to fathead minnow was an LC50 value of 0.115 mg/L (as predicted by Topkat v6.1). This is lower than water solubility estimates for PV29 that EPA provided in the scoping document (0.169 mg/L). This means that PV29 could reach levels in water sufficient to kill 50% or more of fathead minnows exposed to it, not to mention exerting other non-lethal aquatic effects. EPA should not ignore this pivotal toxicity value. (13_120-125)	EPA does not typically rely on modeled toxicity values when empirically-measured toxicity information are available. In the case of PV29, the acute toxicity study with fish indicated that no mortality was observed in test organisms up to the limit of solubility. In addition, the toxicity value used in the screening-level approach described by Environment Canada of 0.169 mg/L is >100x larger than the limit of solubility reported in the water solubility study submitted to EPA in response to the Section 4 Test Order (0.003 mg/L) Nicolaou (2020).
Need to better describe how log K_{oc} was determined		
SACC	SACC COMMENT: • Provide better description of how log K_{oc} was determined in key studies.	The Koc value was derived by using EPI suite estimation software in the Draft Risk Evaluation document. This estimated log K_{oc} using the K_{ow} which has been determined not to be an applicable property for PV29 based on the low solubility in water and octanol. As a result, LogK_{oc} will not be relied upon in the final Risk Evaluation.
Concerns about ecological hazards for sediment-dwelling invertebrates		
SACC, 13, 75, 80	SACC COMMENT: • Include a level of confidence statement with judgements of toxicity to sediment dwelling organisms. PUBLIC COMMENTS: • EPA's conclusion that PV29 is "unlikely to present an unreasonable risk to sediment-dwelling, aquatic invertebrates" is unscientific and unreasonable. (13_132) • EPA noted that PV29 was expected to partition to soil and sediment. Therefore, it cannot conclude there is no unreasonable risk to the environment	The assessment discusses the uncertainties regarding the risk evaluation to sediment-dwelling organisms. The final Risk Evaluation includes an expanded discussion to help understand the level of confidence in the environmental risk assessment for sediment-dwelling aquatic organisms. EPA believes it has adequate hazard data to evaluate the environmental risks of PV29 to aquatic organisms. EPA used the reasonably available data to assess sediment invertebrates. Because PV29 is not expected to sorb to sediment and demonstrates low solubility indicates, the presence in pore water will be low. *Daphnia*, which feed

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	without data on biodegradation and toxicity to benthic organisms. (75_3, 80_5) • Data from a single acute *Daphnia magna* study cannot be used as a proxy to evaluate potential hazards to all sediment-dwelling invertebrates or other organisms. (13_129) • Ankley et al. (1993) provides guidance on assessing the toxicity of sediment-associated contaminants. "For example, many researchers use upper-water-column test species, such as cladocerans (which includes *Daphnia*) and fishes, to assess the toxicity of contaminated sediments; however, these organisms are not relevant if species of concern are benthic, particularly in terms of adequately addressing all possible routes of exposure." (13_131) • See also U.S. EPA, Methods for Measuring the Toxicity and Bioaccumulation of Sediment-associated Contaminants with Freshwater Invertebrates (Mar. 2000) (13_131)	through the entire water column were deemed to be an acceptable surrogate species for sediment invertebrates consistent with EPA/OPP guidance, which lists several considerations for determining the likelihood of exposure and toxicological relevance of exposure to sediment-dwelling organisms (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/toxicity-testing-and-ecological-risk-assessment). EPA appreciates the submission of the sediment-dwelling organism testing guidance (USEPA, 2000). This reference outlines testing procedures for testing with benthic organisms rather than proposing criteria to determine whether this testing is necessary. As EPA did not determine that toxicity data with sediment-dwelling organisms is a critical data need, so this reference was not relevant.
Need for more data to evaluate hazard to terrestrial ecological receptors		
13, 16, 46	PUBLIC COMMENTS: • EPA has not identified any studies of potential terrestrial and avian toxicity for PV29, despite the fact that this substance is persistent and released into the environment, including to landfills where it has potential to leach and contaminate soil. (13_133, 13_109-110, 16_101-103, 46_6) • Toxicity to terrestrial organisms may differ from aquatic organisms. A 2014 ECHA report notes, "Especially for substances with low water solubility toxic effects may not be detectable through acute aquatic toxicity tests whereas	EPA acknowledged the uncertainties in the assessment with regard the lack of hazard data for terrestrial organisms. EPA does not consider this a critical data need because conditions of use are expected to result in limited exposure to terrestrial organisms. Potential exposure to terrestrial organisms resulting from disposal to landfills is expected to be low, as the low solubility of PV29 indicates that leaching from landfill is not likely. In addition, the low bioaccumulative potential of PV29 indicates that releases to water are not expected to biomagnify up the food chain, so exposures to terrestrial organisms under the conditions of use of the assessment are not expected.

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	prolonged aquatic exposure and/or tests with terrestrial organisms exposed through soil or food may result in toxic effects." (13_134-135) • Similarly, a 2014 National Academies report states, "Relative chemical hazards to terrestrial organisms do not necessarily follow the same patterns as that seen with aquatic organisms, necessitating separate testing and assessment schemes." (13_136) • Therefore, the lack of any terrestrial toxicity data for PV29 is a major data gap leading to significant uncertainty. (13_137)	
Concerns about citing the Canadian Ecological Risk Classification for PV29 as support for determination		
13	PUBLIC COMMENTS: • EPA has asserted that PV29 has a low potential for aquatic hazard. In support of this assertion, EPA cited the Canadian Ecological Risk Classification for PV29 (Environment Canada, 2006); however, upon further examination of that source, it does not appear to support EPA's assertion. Canada's categorization exercise was intended only to identify chemicals of potentially high concern, not to also identify chemicals of low concern. In addition, Canadian officials made do with whatever information they already had or could develop rapidly through predictive models. No attempts were made to fill data gaps. Chemicals that Canada found not to meet the categorization criteria should not be characterized as affirmatively low concern. Given the different purpose and limited nature of Environment Canada's analysis, EPA should not	The determinations of potential environmental hazard of PV29 made by EPA and Environment Canada are consistent. Due to the limited nature of the Canadian Categorization results that are publicly available, EPA has removed all reference to the determination by Environment Canada regarding ecological hazard from the final Risk Evaluation.

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	rely on that screening process to support a finding of no unreasonable risk for PV29. (13_115-128) • In EPA's draft risk evaluation, there is mention that Environment Canada made its final ecological risk determination for PV29 using a combination of QSAR modeling and hazard data for analogous pigments with low solubility (*e.g.*, Pigment Red 149). However, neither EPA nor Environment Canada have provided any predicted or measured data for the similar pigments. (13_124)	
Support for EPA's characterization of hazard to ecological receptors		
17, 19	PUBLIC COMMENTS: • No effects were observed in three acute toxicity studies up to the limit of solubility of the chemical. The lines of evidence clearly support EPA's conclusion of low hazard potential to environmental receptors. (17_24-25, 19_8-10) • There are substantial details on ecological hazard data in the studies initially submitted to ECHA and cited by EPA. To enhance clarity in how the data were applied, EPA should consider more clearly linking the robust study summaries available on ECHA's website to the outcome of the risk evaluation. (17_8) • EPA's use of a qualitative approach for ecological exposure assessment is appropriate given the low volume of PV29 material used in finished products (<100,000 pounds) and infrequent use in consumer products. The final risk evaluation should provide additional information on EPA's process for determining the tiered approach it used and why. (17_21)	This is consistent with the approach presented in the final Risk Evaluation. The full study reports for the environmental hazard studies for PV29 have been made publicly available in the docket for PV29, so EPA has removed the references to the ECHA study summaries and has based the conclusions of the risk evaluation on the results of the full study reports. EPA does not have a set guidance for when a risk evaluation utilizes a quantitative or qualitative approach. Instead, the determination is made on a case by case basis as a result of reasonably available data and the potential for a given route of exposure to result in a concern. According to TSCA 702.41(a)(6)-(7): *"(6) The extent to which EPA will refine its evaluations for one or more condition of use in any risk evaluation will vary as necessary to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment.*

#	Summary of Comments for Specific Issues Related to Charge Question 5	EPA/OPPT Response
		(7) To the extent a determination as to the level of risk presented by a condition of use can be made, for example, using assumptions, uncertainty factors, and models or screening methodologies, EPA may determine that no further information or analysis is needed to complete its risk evaluation of the condition(s) of use." In the case of PV29, a comparison of the high-end exposures of PV29 to the available environmental hazard data indicated that risks were not expected and additional quantitative analysis is not necessary.
Concerns about studies where observed exposures exceed water solubility limit		
SACC	SACC COMMENT: • Improve explanations for estimates of toxicity benchmarks developed from those studies where observed exposures exceed the water solubility limit.	The reporting of the solubility limit across the environmental hazard studies is inconsistent. For example, the solubility limit in the Zebrafish study BASF (1988) is reported as 670 mg/l, while the study with *Daphnia magna* BASF (2012) reports a limit of solubility of 0.001 mg/L. This is an uncertainty that is discussed in the final Risk Evaluation. Following the publication of the draft risk evaluation U.S. EPA (2018b), EPA identified the uncertainty regarding the limit of solubility of PV29 in octanol and water as a critical data gap for the assessment and issued a TSCA Section 4(a)(2) Test Order for C.I. Pigment Violet 29 on February 28, 2020. These data were submitted to the agency and confirm the low solubility of PV29 in both octanol and water (<0.003 mg/L). The submission of these data clarifies the uncertainties regarding the solubility.

Human Health

Charge Question 6.a: Please comment on the toxicological study which was used to identify the endpoint of concern and derive the associated point of departure (POD). Also, please comment on alternative approaches to estimate the potential for lung effects using analogs for poorly absorbable particles to calculate an inhalation toxicity POD and the screening-level calculation to estimate the potential for lung overload. Please comment on this approach and whether this analog represents useful information to quantify risk for the inhalation route and whether oral developmental study is appropriate for all routes of exposure. If not, please describe what other alternative approaches could be used in lieu of these approaches to serve as the basis for completing the hazard assessment and subsequent risk evaluation for PV29.

Charge Question 6.b: Please comment on the use and interpretation of Multiple-Path Particle Dosimetry Model (MPPD v. 3.04), which has not been formally peer-reviewed, to predict lung deposition of aerosolized PV29.

Charge Question 6.c: Please comment on the evidence available to support the agency's conclusion of negligible absorption via oral, dermal, and inhalation routes.

Charge Question 6.d: Given the varied nature of the consumer uses, please comment on the agency's characterization of hazard to consumers via inhalation and dermal exposure for different durations of exposure.

Charge Question 6.e: Similarly, please comment on the Agency's characterization of hazard to workers via inhalation and dermal exposure for different durations of exposure.

Charge Question 6.f: Please comment on the Agency's consideration of health hazard concerns for potentially exposed susceptible subpopulations given the constraints of the available information (*e.g.*, children, workers, or pregnant women).

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
Support for EPA's approach and conclusions regarding human health risk		
19, 47, 49	PUBLIC COMMENTS: • EPA's health hazard determination and decision that guideline studies for each human health endpoint are not necessary for risk determination are adequately supported with data regarding genotoxicity, SARs, and poor absorption. (19_8, 19_13) • EPA appropriately concluded that it did not need to possess a guideline study of PV29 regarding every conceivable human health endpoint. (19_13) • EPA's cross-route extrapolation of oral route exposure to derive other no-observable adverse effect levels (NOAELs) to address systemic effects is appropriate and is a typical convention of risk assessment practice. (47_2) • The summaries of the 10 short-term assays provided sufficient information and show compliance with OECD test guidelines. (49_7)	EPA acknowledges these comments and encourages the commenters to consult the final Risk Evaluation for the most updated risk characterization.
Make hazard conclusions specific to routes of exposure		
SACC	SACC COMMENTS: • Wherever in the Evaluation the statement "PV29 has low hazard potential across all possible routes of exposure" occurs, the statement should be replaced with one that is specific and limited to the routes of exposure observed in the available study data—thus allowing new data, as it becomes available, to add to and expand hazard conclusions regarding PV29.	EPA acknowledges this and has updated the language in the final Risk Evaluation to better tie the risk determinations ot the specific conditions of use of PV29. Statements on low exposure when EPA lacks the data were updated where necessary.

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
Clarify value of the screening reproductive/developmental toxicology study and highlight data gaps		
SACC	SACC COMMENTS: • Include a table in the Evaluation that compares the endpoints reported in the screening reproductive/developmental toxicological study used in the Evaluation to endpoints typically reported in a 90-day subchronic toxicity study or to compare what's available for PV29 versus a basic SIDS data set–to clarify the value of the screening reproductive/developmental toxicological study and highlight data gaps in the toxicity assessment.	EPA did not make this change. There is no minimum data set for risk evaluations conducted under TSCA. EPA obtained all reasonably available data for C.I Pigment Violet 29 and issued a TSCA Section 4(a)(2) Test Order for C.I. Pigment Violet 29 to address critical data gaps in the assessment. Other data gaps, such as environmental hazard testing with aquatic species and inhalation toxicity testing, were addressed by using analogue toxicity data or with QSAR modeling.
The toxicity studies EPA used are unreliable		
8, 10, 12, 13, 14, 16, 46, 48	PUBLIC COMMENTS: • EPA uses unacceptable and unreliable studies that present risk of bias to determine inhalation toxicity and chronic health effects and the measurements use for PV29 levels are unreliable. (10_2, 16_84, 48_10, 48_15) • The OECD 421 screening test utilized is flawed and unreliable. It cannot be used to estimate human risk. (12_27, 13_148, 13_191, 14_8, 14_16, 16_84) • EPA cannot determine reproductive toxicity hazard based on the current data available and should provide more discussion on reproductive toxicity screening limitations. (8_17, 10_9, 14_12) • There are concerns with the quality ratings of the oral toxicity studies due to inadequacies,	The ranking of data sources in the Risk Evaluation is reflective of the approaches outlined in *Application of Systematic Review in TSCA Risk Evaluations.* EPA is in the process of seeking peer review of its Systematic Review protocol, and potential bias of data sources may be addressed in future updates. EPA believes that OECD 421 is adequate to determine whether additional reproductive testing is necessary. As no significant adverse effects were observed in the study, EPA believes that this provides justification that no additional reproductive testing is necessary. To alleviate concerns about the oral toxicity studies, EPA has released the partially redacted study reports and the updated systematic review data quality evaluation scoring sheets to the PV29 Docket (EPA-HQ-OPPT-2018-0604)

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
	information gaps, and a protocol that is no longer available online for evaluation. (48_8) • Multiple studies utilized by EPA are inadequate, such as the 10-page report prepared by BASF providing summaries for 10 studies which lack supporting data, and the developmental toxicity study which involved a small number of rats from a single species. (12_28, 14_8, 46_2)	EPA acknowledges that the study reports are often truncated and overly summarized. As this represents the best available data to understand the potential health effects of PV29, EPA utilized the study report results to understand the human health hazards of PV29 and issued a Section 4 Test Order where critical data were considered insufficient.
EPA improperly disregarded intraperitoneal studies		
12, 13, 16	PUBLIC COMMENTS: • EPA improperly disregarded intraperitoneal studies reporting clinical effects and death. These two studies should not have been rejected as irrelevant but instead treated as reliable because there is a strong scientific basis for treating intraperitoneal dosing studies similarly to oral dosing studies. (12_25, 16_8, 16_57, 16_63, 16_70) • EPA swiftly discounts evidence of hazard. Toxic effects were observed in intraperitoneal studies, but EPA invoked its problematic low solubility argument. EPA cannot rely on a deeply flawed low solubility-low absorption argument to dismiss the observed effects those studies. (13_147)	EPA released an update to the systematic review supplemental file that provided the reviewer comments and updated systematic review data quality evaluation scores in response to comments received from the public. These files are available on the docket for PV29 at: https://beta.regulations.gov/document/EPA-HQ-OPPT-2018-0604-0040 The result of this data quality evaluation found that the intraperitoneal injection studies were of low quality but were not used qualitatively in the evaluation. As stated in the final Risk Evaluation, the studies were not used in the screening level risk evaluation because the route of exposure (intraperitoneal injection) is not a relevant route of exposure for PV29, so there is a great deal of uncertainty about how this exposure pathway relates to the routes of exposure expected for C.I. Pigment Violet 29. In addition, the concentrations where adverse effects were observed in the test animals (LD_{50}= 7000-9000 mg/kg-bw) is far greater than the NOAEL for reproductive/developmental toxicity of 1000

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
		mg/kg-bw that was used in the screening-level risk evaluation.
EPA did not use data from similar substances		
13, 15	PUBLIC COMMENTS: • EPA failed to utilize data on similar substances. (15_2) • An analysis of PV29 through ToxTree provides a structural alert for PV29 given its structural similarity to polycyclic aromatic hydrocarbons (PAHs). EPA completely fails to analyze this structural alert or consider this evidence suggesting that PV29 may be a carcinogen as a result of this similarity. (13_152)	EPA has updated its approach in the final Risk Evaluation to incorporate analogue toxicity data into the screening level risk evaluation for inhalation exposure. Empirical data indicates that C.I. Pigment Violet 29 is negative for genotoxicity and Structural activity relationships (SAR) considerations support EPA's conclusion that C.I. Pigment Violet 29 is unlikely to be a carcinogen. Given the low potential for biodegradability, the relevance of PAHs as a predictor of carcinogenicity are low.
EPA should acquire additional studies due to insufficient data		
SACC, 10, 12, 13, 14, 15, 16, 18, 22, 43, 46, 49, 74, 75, 76, 82	SACC COMMENTS: • 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. • The utility of the screening reproductive/developmental toxicological study for deriving the POD would benefit from additional and better estimates of physical/chemical properties and ADME studies to further strengthen support that PV29 has low bioaccessibility/bioavailability and therefore, decreased risk for absorption and inhalation. PUBLIC COMMENTS: • There is insufficient data to make a human health hazard determination due to CBI and insufficient	To address the uncertainties identified in the assessment, EPA has issued a TSCA Section 4(a)(2) Test order for the development and submission of additional solubility testing of C.I. Pigment Violet 29 in water and octanol. This solubility testing has been submitted to EPA, and it was determined to be high quality and acceptable for use in this risk evaluation. This reduces the uncertainty about the preliminary determination that the low solubility of C.I. Pigment Violet 29 results in a low potential for absorption. To further reduce uncertainties related to the screening-level risk analysis of inhalation exposure, EPA decided to use analogue toxicity data to better characterize the hazards to workers from chronic inhalation of C.I. Pigment Violet 29. While there are uncertainties regarding the available data for C.I. pigment Violet 29, EPA has determined that sufficient

	testing, including the following topics: PV29 levels, exposure characteristics, absorption, and chronic toxicity. (13_6, 13_7, 13_90, 13_98, 13_101, 13_165, 14_16, 15_2, 16_74, 46_6, 74_2, 76_3, 82_1) • EPA has authority to acquire more "reasonably available data" by requiring additional studies by manufacturers to evaluate human hazard. (10_3, 12_4, 13_90, 13_146, 13_194, 14_14) Specific suggested study types that should need to be included are: – High-quality, reliable experimental test results for acute inhalation toxicity. (16_9) – A 90-day repeated dose toxicity study for oral, inhalation, and dermal routes of exposure. (16_9, 49_4, 10_3, 13_284) – Chronic mammalian health studies sufficient to account for exposures via dermal, inhalation, and oral routes. (18_8, 10_3, 13_284) – Carcinogenicity studies. (10_3, 12_22, 14_14, 16_9) – Respiratory/inhalation sensitization studies. (12_22, 10_3, 16_88) – Tests for genetic toxicity/mutagenesis/gene mutation, including in vivo tests for chromosome damage, cytotoxicity, and other relevant endpoints. (10_3, 14_14, 16_9) – Neurotoxicity studies, including developmental stages. (10_3, 12_22, 14_14, 16_88, 16-9) – Two generation reproduction toxicity studies. (10_3, 12_22, 16_9)	data exist to make a risk determination for C.I. Pigment Violet 29 under the conditions of use of the assessment. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation. However, EPA will continue to improve on its method and data collection for the next round of chemicals to be assessed under TSCA.

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
	– Studies for acute and chronic endocrine effects. (10_3, 12_22, 14_14, 16_9) – Pharmacokinetic study measuring distribution in blood and fat and toxicokinetic studies. (10_3, 16_88, 75_2)	
Increase transparency of evidence used to determine carcinogenic risk		
8, 17	PUBLIC COMMENTS: • EPA should provide more detail on the in vitro carcinogenicity assessment, including a description of the structure-activity relationship (SAR) data/programs that were used, how they were evaluated, and why the data strengthens confidence in a low likelihood of carcinogenic risk. In addition, EPA could further describe how the assessment of carcinogenicity includes consideration of other available in vivo toxicity studies, in particular, the evaluation of histopathology in repeat dose studies. (17_23, 8_15)	The SAR determination for carcinogenicity was based on expert judgement about the carcinogenic potential of functional groups to elicit carcinogenic potential. This determination is supported by the available data for C.I. Pigment Violet 29, which was considered in the assessment. This information has been captured in the OncoLogic™ predictive model which is available at: https://www.epa.gov/tsca-screening-tools/oncologictm-computer-system-evaluate-carcinogenic-potential-chemicals
Concerns about route-to-route extrapolation and lack of uncertainty factor		
10, 12	PUBLIC COMMENTS: • EPA incorrectly determined low hazard across all routes of exposure and used an oral exposure study to calculate the point of departure for its analysis of dermal and inhalation risks, but this extrapolation ignores the potential that PV29's absorption rate is lower for oral exposures than for inhalation and an uncertainty factor should have been applied. (10_11, 12_33)	EPA acknowledges the uncertainties inherent in utilizing a route-to-route extrapolation to assess the risks from inhalation exposure. As a result, EPA has updated the risk characterization for inhalation exposure to use chronic inhalation toxicity data for carbon black to represent the inhalation toxicity for C.I. Pigment Violet 29 following chronic exposure.

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
MPPD model requires size distribution of PV29 in workplace aerosols		
77	PUBLIC COMMENTS: • The MPPD model depends on the particle size distribution, but EPA lacks data on the size distribution of PV29 particles in workplace aerosols. (77_3)	Through correspondences with the sole US manufacturer of C.I. Pigment Violet 29, EPA has obtained additional characterizations of the particle size of C.I. Pigment Violet 29 dust that can represent the potential workplace exposure of C.I. Pigment Violet 29 dust. These particle size distributions have been be made public with the final Risk Evaluation as a supplemental file, titled, "*Supplemental File: Information Received from Manufacturing Stakeholders* U.S. EPA (2020a)."
Present models or NAMs to improve understanding of absorption potential		
SACC	SACC COMMENTS: • Given the low confidence in absorption potential based on limited physical-chemical data, present models based on several solubility scenarios or NAM in vitro testing using tissue adsorption models.	To address the uncertainties identified in the assessment regarding the assumptions made about the absorption potential of C.I. Pigment Violet 29 from its solubility, EPA issued a TSCA Section 4(a)(2) Test order for the development and submission of additional solubility testing of C.I. Pigment Violet 29 in water and octanol. This testing was received and reviewed by the agency and found to be of high quality. As a result, EPA has high confidence that the data received as a result of the Section 4 Test Order represents the true limit of solubility of PV29.
Concerns about lack of scientific evidence for EPA's conclusion regarding absorption potential		
8, 12, 13, 16, 18, 46, 55, 77, 78	• EPA has no scientific basis for using low solubility to conclude there would be no absorption through the dermal and inhalation routes of exposure, but did not provide confirmatory data, which could have been readily obtained using EPA's section 4 testing authority.	As indicated above, EPA issued a TSCA Section 4(a)(2) Test Order for the submission of water and octanol solubility studies to reduce uncertainties about the available data used in the Draft Risk Evaluation. EPA determined that the low solubility in water and octanol initially reported in the assessment and confirmed by the studies submitted as a result of the Section 4 Test Order was

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
	(12_25, 13_6, 13_102, 13_162, 13_165, 16_7, 16_45, 16_62, 18_11, 46_6, 77_3, 78_6, 55_5) • EPA should consider basic physicochemical information (*i.e.*, molecular mass and lipophilicity) when determining dermal absorption. EPA ignored the multiple mechanisms by which chemicals, including poorly soluble substances, may be absorbed. EPA should have obtained actual absorption information instead of simply assuming that low solubility will necessarily result in low absorption. (13_103) • EPA did not consider how the presence of other constituents in a PV29 formulation, such as surfactants, can significantly alter the absorbability of PV29. (13_164) • EPA assumes that a lower fraction of PV29 is dermally absorbed than the source it cites as support recommends based on the chemical's properties. (13_8) • Given the inconsistency in the way exposure potential is described, OPPT should clarify exposure assumptions, specifically with regards to applying a consistent approach regarding potential for dermal absorption. (8_12)	adequate evidence to conclude that absorption of PV29 is low. As there are limited data to indicate that components of the formulations can affect the absorbability of PV29, EPA acknowledges that there are uncertainties about this issue. Given the difficulty of finding a solvent for PV29, it is likely that the stability of the compound is high in all but highly acidic conditions. EPA has updated the final Risk Evaluation to remove the screening level risk evaluation for dermal exposure presented in the Draft Risk Evaluation. The overly conservative nature of the assumptions in that approach and the route to route extrapolation using the subchronic NOAEC to calculate an MOE for dermal and inhalation hazard meant that the results were of limited utility to actual exposure scenarios, especially for a substance that is as poorly absorbed as PV29. Therefore, the discussion of the inputs used in that approach are no longer relevant.
Consumer hazard is not fully investigated		
SACC 12, 13	<u>SACC COMMENTS:</u> • Improve the discussion of the uncertainty surrounding exposures for the general population. Explain clearly why it was initially determined that there were widespread consumer exposures to	EPA acknowledges the uncertainties in its conclusion that risks are not expected for the general population. EPA has high confidence in this conclusion, as a high percentage of PV29 is used as an intermediate and is therefore converted into other chemical substances and is therefore not released

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
	PV29 but that this did not need to be addressed in the final risk assessment. Clearly acknowledge that there may be certain consumers that receive higher acute and chronic exposures and explain why this is not considered important for this risk assessment. PUBLIC COMMENTS: • EPA does not provide evidence to support the expectation that consumer and general population exposures will be lower than worker exposures. (12_20, 13_6) • EPA has not fully evaluated hazards to consumers. (12_8, 13_244) • EPA cannot expect that consumers exposed to PV29 will wear protective gear. (13_185)	into the environment. Therefore, PV29 exposure is primarily expected to result in a manufacturing setting and not as a result of exposures to consumers and the general population from downstream uses. Based on the available data to characterize consumer exposures to PV29, the consumer uses are not expected to result in long term inhalation exposure to PV29 dust, which is the primary route of concern for PV29. Exposures from this pathway are expected to result from manufacture, processing and industrial/commercial uses to workers. Regardless, the risk evaluation is updated to better explain potential risks to consumers. EPA calculated risks from occupational exposures with and without the use of PPE. EPA does not assume that consumers will use PPE.
Obtain more occupational hazard data		
SACC 13	SACC COMMENTS: • Clearly acknowledge that there are few data to support a confident conclusion that workers would not be exposed, and therefore, not experience human health hazards via dermal and/or inhalation routes. • Obtain and incorporate into the Evaluation better (*e.g.*, collected using standard measurement techniques with adequate temporal and spatial coverage) data/documentation from the	Uncertainties were identified regarding reasonably available information characterizing PV29's occupational worker inhalation exposure. These uncertainties have resulted in EPA requiring testing of PV29 to develop new information in order for EPA to increase certainty in the final Risk Evaluation of PV29 under TSCA section 6(b). Test data was reviewed for data quality according to the relevant data quality evaluation metrics and incorporated into the final Risk Evaluation. This information includes information that measures exposures to workers from the sole US manufacturer of C.I. Pigment Violet 29.

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
	manufacturer on conditions of use, exposures, and potential for worker exposures. • Regardless of whether PV29 is bioavailable, more justification is needed to conclude that exposures to dusts in occupational settings do not cause lung depositional events or immunological responses sufficient to cause injury. PUBLIC COMMENTS: • Manufacturers must submit all available information on occupational hazard and exposure under the identified conditions of use because EPA must consider all hazards and exposures when preparing risk evaluations. (13_258)	The updated human health risk evaluation for C.I. Pigment Violet 29 calculates an updated POD based on the potential for lung depositional events based on lung overload observed in an analogue, carbon black Elder et al. (2005). All information gathered from correspondences with industry stakeholders regarding PV29 is being made publicly available with the final Risk Evaluation as a supplemental file, titled, "*Supplemental File: Information Received from Manufacturing Stakeholders* U.S. EPA (2020a). In addition, where occupational exposure information was judged to be insufficient, EPA issued a Section 4 Test Order for the generation of workplace dust monitoring data. These data are used in the final Risk Evaluation to estimate workplace exposure to PV29 dust.
Clarify uncertainties and justify conclusions regarding susceptibility		
SACC 8, 9, 10, 12, 13, 14, 16, 77, 78, 82	SACC COMMENTS: • Clarify the statement in 3.4.1, "there is no evidence of increased or decreased susceptibility for any given population" to acknowledge that there are large data gaps that preclude coming to confident conclusions regarding certain subpopulations. • Do not make statements without additional clarifications and justifications that children or other susceptible populations would be protected. The current data as discussed in the data integration does not clearly support this conclusion and the committee has recommended	EPA acknowledges the uncertainties regarding this conclusion and has updated the final Risk Evaluation to explain these uncertainties EPA has identified critical data needs and issued a Section 4 Test Order to fulfill these needs. As a result, EPA received additional information and incorporated it into the evaluation. EPA has modified the risk characterization approach to better represent the expected effects of exposure to PV29. While there are remaining uncertainties, EPA is confident that its risk determination is protective of potentially exposed or susceptible subpopulations identified in this risk evaluation.

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
	additional data needs and rationale to address this uncertainty. Some committee members recommended EPA consider an "indeterminate" categorization and qualify with data that may suggest low toxicity. Methods to address this would include using more uncertainty factors in MOE calculations or developing multiple modeling scenarios including best case to worst case and presenting these models in the text. • Improve transparency by acknowledging in the evaluation that there are no data supporting the determination of hazards or exposures to children or other susceptible populations on which to make confident conclusions regarding risk to these susceptible subpopulations. <u>PUBLIC COMMENTS:</u> • EPA has not met the TSCA mandate to consider risks to PESS and needs to require additional studies and data collection. (10_12, 13_7, 13_191, 13_287, 14_20, 77_5) • The agency did not adequately consider pregnant women, children, and other vulnerable subpopulations, those vulnerable in the workplace, and should apply uncertainty factors in their hazard assessment. (8_18, 9_2, 10_12, 12_20, 12_34, 13_191, 78_8, 82_3) • A factor of 10 is applied for risk assessments on dietary pesticide ingestion for PESS. (10_12) • EPA should seek the advice of its Children's Health Protection Advisory Committee. (16_22)	EPA has updated the risk evaluation to discuss uncertainties resulting from lack of data for specific susceptible subpopulations including children and other susceptible populations outlined in Section 2.4.1.

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
There are no vulnerable subpopulations		
45	PUBLIC COMMENTS: • There are no vulnerable subpopulations with reasonably foreseen exposures to harmful quantities of PV29. Workers in U.S. manufacturing facilities do not constitute a vulnerable subpopulation. (45_7)	EPA has updated the risk evaluation to discuss uncertainties resulting from lack of data for specific subpopulations.

Risk Characterization/Risk Determination

Charge Question 7.a: Please comment on whether the information presented to the panel supports these conclusions outlined in the draft risk characterization section concerning PV29. If not, please suggest alternative approaches or information that could be used to develop a risk finding in the context of the requirements of EPA's final rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726).

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
Support for the conclusions in the draft risk characterization		

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
17, 19, 47	PUBLIC COMMENTS: • The risk evaluation relies on conservative, lower-tier screening approaches to risk assessment to support the determination that PV29 does not pose an unreasonable risk of harm to human health or the environment under reasonably foreseeable conditions of use. This is appropriate due to PV29's evidence of low toxicity, largely industrial conditions of use, and low volume of material used in finished products. (17_3, 19_3) • EPA appropriately considered the full body of toxicity studies, physical-chemical properties, use patterns and relevant routes of exposure, addressed uncertainties, and used an established health-protective approach to calculate risks that accounts for the different routes of exposure. EPA utilized conservative assumptions and highly protective default values for risk characterization. Even so, EPA found no unreasonable risk. (17_26, 19_7-10) • EPA collected more than enough data to support its risk evaluation and appropriately concluded that a guideline study is not needed for every conceivable human health endpoint. EPA's conclusions confirm those contained in the published EU Registration, Evaluation and Authorization of Chemicals (REACH) summaries. Further assessment of PV29 would not yield any benefit for EPA, consumers, industry or workers. EPA's limited risk evaluation resources should be directed to substances for which	EPA acknowledges the comments and has incorporated the suggestions received in these comments where applicable.

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
	reasonably foreseeable conditions of use pose a high potential for unreasonable risk. (19_11-15) • Despite the changes to these quality scores [after the first round of comments], the risk evaluation is not impacted for the following reasons. First, high-quality studies also exist for both acute oral toxicity and eye irritation. Second, EPA has evaluated the remainder of the studies used for the risk evaluation to be of medium- and high-quality, including biodegradation and aquatic toxicity studies, which address the limited water solubility. Third, EPA uses the high-quality reproduction/developmental toxicity study to identify the no-observed-adverse effect level (NOAEL) that is used in the MOE calculations. (47_1)	
The conclusions in the draft risk characterization are flawed due to lack of data		
SACC, 10, 11, 12, 13, 14, 16, 44, 46, 55, 74, 75, 77, 80	SACC COMMENTS: • Saying that no unreasonable risks for PV29 were identified may reflect the weakness and limitations of the database. • Lack of evidence isn't evidence. [Note: refers to data gaps.] PUBLIC COMMENTS: • EPA relied on inadequate hazard and exposure data to determine that PV29 does not present an unreasonable risk of injury to human health or the environment. In addition, the draft risk evaluation	EPA had sufficient information to complete the PV29 risk evaluation using a weight of evidence approach. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation. However, EPA will continue to

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
	contains numerous logical flaws and unwarranted assumptions, rendering its final conclusion unsupported by substantial evidence, as required under TSCA. The resulting draft risk evaluation fails to consider reasonably available information or to use the best available science. (10_2, 11_17, 12_22, 13_3, 13_55, 13_110, 13_144-146, 14_6, 16_25, 16_65, 16_110, 44_18, 46_6, 46_27, 55_10, 74_2, 77_2, 80_2) • A lack of information does not mean that there is no or low exposure or hazard. EPA improperly inferred the absence of risk from the absence of information. (12_4, 13_14, 13_146) • EPA has based its conclusion of "no unreasonable risk" on claims of low exposure, low bioavailability, and low toxicity observed only in short-term studies. These data seem to support a hypothesis of low risk but are woefully insufficient to establish it. (75_2) • EPA concludes that PV29 is not carcinogenic on the basis of insufficient information and unsupported assumptions. (12_22, 13_7, 13_151, 14_13, 16_68-69, 46_6) • The new information that has now been made available [referring to the release of the full studies] further demonstrates the poor quality and limited scope of the data in the draft evaluation and underscores the lack of evidence to support a finding that PV29 does not present an unreasonable risk of injury. (55_1)	improve on its method and data collection for the next round of chemicals to be assessed under TSCA. To address the uncertainties identified in the assessment regarding the assumptions made about the absorption potential of C.I. Pigment Violet 29 from its solubility, EPA issued a TSCA Section 4(a)(2) Test order for the development and submission of additional solubility testing of C.I. Pigment Violet 29 in water and octanol. This testing has been received and reviewed by the agency and found to be of high quality.

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
EPA should order the development and submission of additional information		
SACC, 9, 55, 76, 77, 80, 82	SACC COMMENTS: • If it is not possible to arrive at an "indeterminate" conclusion, EPA could conclude that the limitations in the data are sufficient to conclude an "unreasonable risk" and, as a regulatory response, order the manufacturer to develop a limited set of new data, the development of which would not be time limited. • The Agency needs to compel answers to these questions if they are to accurately assess the potential human and environmental hazards. Such questions include long-term effects of PV29 exposure, apparent lack of consensus regarding PV29 solubility, and data gaps regarding characteristics and fate of PV29. PUBLIC COMMENTS: • The Agency had ample opportunity to use TSCA authorities to obtain additional hazard and exposure data that could have supported a defensible risk evaluation – as Congress intended – yet refused to do so, instead reaching categorical conclusions about the absence of risk that simply cannot be supported by the inadequate data in the record. (9_2, 55_1, 76_4, 77_1, 80_4, 82_2-3)	In response to uncertainties resulting from lack of data identified in public and SACC comments, as well as in the risk evaluation, EPA issued a TSCA Section 4(a)(2) Test Order for C.I. Pigment Violet 29 on February 28, 2020. This test order compelled the creation and submission of three studies by the sole U.S. manufacturer of PV29, Sun Chemical Corporation to address critical data gaps identified in the risk evaluation. EPA is currently working to identify data deficiencies earlier in the prioritization/risk evaluation process. TSCA section 6 requires EPA to determine within a specified period of time whether a chemical substance presents an unreasonable risk of injury to health or the environment. The uncertainties identified were in regard to reasonably available information characterizing PV29's solubility and occupational worker inhalation exposure. Test data were received and reviewed for data quality according to the relevant data quality evaluation metrics and incorporated into the final Risk Evaluation. The studies received by EPA in response to this Section 4 order included solubility of PV29 in water and octanol, as well as a workplace monitoring study of particles not otherwise regulated, conducted according to the NIOSH 0600 guideline. More information about this test order can be found at: https://beta.regulations.gov/document/EPA-HQ-OPPT-2020-0070-0008
EPA's reliance highly uncertain fate and persistence information casts doubt on its risk conclusions		

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
13, 46, 55	PUBLIC COMMENTS: • EPA fails to acknowledge and address serious limitations and uncertainties associated with several of its characterizations of PV29's physical-chemical and environmental fate properties that it relies on to conclude low risk. (13_4) • EPA relies heavily on a single, poorly documented value for water solubility while failing to account for other available data on water solubility. This reliance on a highly uncertain value casts major doubt on all of EPA's risk conclusions. (13_4, 13_36, 55_17) • EPA's risk conclusions fail to address the implications of the very high persistence of PV29 in the environment. EPA relies upon modeled values derived using an estimation program lacking sufficient data on similar chemicals. (13_4, 46_6, 55_17)	As discussed above, EPA issued a TSCA Section 4(a)(2) test order to generate more data that address uncertainties related to the physical-chemical properties of C.I. Pigment Violet 29, particularly the uncertainty regarding the solubility studies. These solubility data were used to reduce uncertainties stemming from the low confidence ratings of the solubility data presented in the draft Risk Evaluation. EPA acknowledges the persistence of PV29, but based on the low potential for bioaccumulation and low toxicity, the persistence does not result in specific risk concerns.
Criticism of the margin of exposure (MOE) approach and clarity		
SACC 8, 10, 12, 14, 16, 46, 48, 77	SACC COMMENTS: • Either do not perform MOE calculations or clearly qualify assumptions used in the MOE calculation based on the limited data. PUBLIC COMMENTS: • EPA should not use MOE as an analysis method in the risk evaluation process. MOE is not an estimate of risk, it is a single number that is a version of the "bright line" approach. This approach does not provide information about the magnitude of the risks above, at, or below the line. Further, it implies	EPA acknowledges these comments and has attempted to explain the additional assumptions used in the calculations of the MOEs used in the final Risk Evaluation. This includes selecting uncertainty factors that are more appropriate given the limitations of the reasonably available data for PV29. To increase transparency, EPA has compiled the available data received from the sole US manufacturer, Sun Chemical, and used in the risk evaluation into a single

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
	that there is a "safe" level of exposure below which no harm will occur. While this may be true for a select few chemicals, the NAS Science and Decisions report recognizes that this is not a valid assumption for all chemicals and has recommended moving away from such "bright line" approaches which do not establish risk estimates across the full range of exposures. Additionally, the MOE will not provide the necessary information for future analysis of risks and benefits that will be critical for decision-making on these chemicals. We recommend that EPA utilize available analytical methods, such as PODs based on a Benchmark Dose, to develop quantified estimates of risk. (14_15-19) • The results from the MOE approach does not adequately account for humans that may be more susceptible to chemical toxicity, and an uncertainty factor should be considered. (10_7, 12_34, 16_37) • EPA incorrectly relied on a single studies or data points to base elements of their risk determination. (46_6, 77_5) • In response to FOIA requests and our initial comments, EPA has failed to provide any supporting data or other justification for the critical workplace air concentration on which its MOE calculation is based, further weakening its assertion that workers and other exposed populations are not at risk of harm. (48_1)	supplemental file. This supplemental file has been uploaded to the docket with the final Risk Evaluation.
Supports EPA's use of the MOE approach		

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
17	• The PV29… MOE assessment is evidence of the utility of EPA's risk assessment approach in appropriate cases. (17_4) This commenter supports EPA's use of an MOE approach to assess non-cancer risk. (17_26)	EPA acknowledges the comment and encourages the commenter to consult the updated risk characterization approaches in the final Risk Evaluation.
Concerns about CBI affecting the risk characterization		
SACC	SACC COMMENTS: • EPA should continue to encourage data submitters to review CBI claims closely prior to submission. • EPA should consider novel ways to make full study reports available to interested members of the public without compromising the investment of the data owner.	EPA understands the uncertainties that arise when data are not publicly available due to CBI claims. EPA will work with stakeholders to ensure that relevant data are made available while adhering to the applicable legal requirements regarding confidential business information.
Need to apply additional uncertainty factors		
8, 10, 12, 13, 77, 80	SACC COMMENTS: • Include the subchronic-to-chronic uncertainty factor in the calculations of the MOE or significantly improve the justification/qualifications in the Evaluation for why this uncertainty factor should not be used. PUBLIC COMMENTS: • EPA failed to apply the necessary uncertainty factors to account for the many data gaps in the PV29 human hazard database of studies. (10_6, 12_29, 13_8, 77_6-7) • Additional 10-fold uncertainty factors that EPA should have considered include: database deficiencies, extrapolation from short-term to chronic exposures, extrapolation from oral to	EPA updated the risk evaluation so that the route to route extrapolation used to characterize risks from inhalation and dermal exposure of PV29 presented in the Draft Risk Evaluation is no longer included in the final Risk Evaluation for human health. In place of this assessment, which was determined not to be appropriate based on feedback provided through public and interagency comments, EPA has chosen to focus on the effects of lung overload following chronic exposure to PV29. Based on available data characterizing the effects of particles with a similar size, density and solubility, the most relevant effect from inhalation of PV29 is the overloading of lung clearance mechanisms. As a result, the discussion of the application of uncertainty factors to the subchronic oral NOAEC to calculate an MOE is no longer relevant. Discussions about the use of assessment factor in this

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
	inhalation and dermal exposures, and vulnerable subpopulations (pregnant women, infants and children). (10_9-12, 12_30-34, 80_3) • EPA OPPT should use an adjustment factor for intraindividual variability. (8_18) • EPA used an oral exposure study to calculate the point of departure for its analysis of dermal and inhalation risks, but this extrapolation ignores the potential that PV29's absorption rate is lower for oral exposures than for inhalation and an uncertainty factor should have been applied. (10_11, 12_33) • Even adding a single additional uncertainty factor would result in a benchmark value exceeding the MOE that EPA calculated for worker dermal exposure. (13_8) • If EPA had applied all of the appropriate uncertainty factors, the benchmark MOE would have far exceeded the acceptable margins of exposure and EPA would have concluded that PV29 presents an unreasonable risk to human health. (10_13, 12_35)	assessment have been included in Section 4 of the final Risk Evaluation where necessary.
Use of intraspecies uncertainty factor was conservative		
8	PUBLIC COMMENTS: • The point of departure (POD) was selected from a reproductive and developmental screening study. Considering this study design evaluates hazards to potentially sensitive subpopulations, an additional factor for interindividual variability may not be necessary. We request OPPT acknowledge the conservatism of this approach and consider potential	EPA acknowledges the uncertainties regarding this approach as well as the potential for conservative assumptions.

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
	redundancy in adjustments for sensitive populations via an adjustment factor for intraindividual variability. (8_18)	
Occupational risk characterization is flawed		
11, 12, 13, 18	PUBLIC COMMENTS: • It is wrong and inconsistent to use personal protective equipment (PPE) and safety data sheets (SDSs) as a baseline for risk determination. Risk should be assessed on the basis of health impacts. PPE is not a basis for risk; it is a means to control the risk. There is no OSHA requirement for employers to follow the recommendations of SDSs. (11_7-8, 18_12) • EPA should mandate worker protections for PV29 consistent with agencies specializing in occupational safety and health regulation and research (*e.g.*, OSHA and NIOSH). (18_5) • Even with using one uncertainty factor for dermal exposure, EPA cannot conclude that PV29 does not present an unreasonable risk to workers. (13_208)	EPA's approach for developing exposure assessments for workers is to use reasonably available information and expert judgement. EPA considers each condition of use and constructs exposure scenarios with and without PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. For the purposes of determining whether a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on this information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in Section 5.2. While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in Section 5.2. EPA has consulted with NIOSH to update the inhalation risk characterization to ensure that the evaluation follows the best practices for risk assessment.

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
		EPA updated the approach to characterize the risks of dermal exposure to PV29. This screening level assessment of risks from dermal exposure presented in the draft Risk Evaluation were extremely conservative and not representative of actual exposure under the conditions of use of the assessment.
Need to expand the risk characterization narrative		
8	PUBLIC COMMENTS: • EPA did not sufficiently describe the thought process and rationale that led to the conclusion of no unreasonable risk for PV29. There are concerns about how this method will be applied to future chemical risk evaluations. OPPT should expand the narrative in the risk evaluation document to more clearly describe how the available information supports its findings, particularly with regard to determining that the evidence was sufficient for a risk determination. (8_6-19)	To increase the transparency and clarity of the process used to arrive at the risk determinations, EPA tied each risk determination in the final Risk Evaluation for PV29 to a condition of use and explained the uncertainties involved.
Need additional guidance on when higher-tier assessments will be triggered for future risk evaluations		
17	PUBLIC COMMENTS: • Additional guidance, developed with stakeholder engagement, would be helpful for future risk evaluations, especially regarding tiered approaches to assessment, occupational exposure assessment, and systematic review. In particular, additional guidance from the Agency on how and when higher-tier assessments will be triggered would be helpful for future risk evaluations. (17_26-31)	As discussed above, in Section 4, EPA is not planning to develop a guidance for a tiered approach to Risk Evaluation. Each chemical is assessed using a fit-for-purpose approach that depends on the reasonably available information and conditions of use specific to each chemical. This is consistent with the flexibility afforded to EPA for this risk evaluation process, as explained in 40 CFR 702.41(a)(6) and (7), which explains:

#	Summary of Comments for Specific Issues Related to Charge Question 7	EPA/OPPT Response
		(*6) The extent to which EPA will refine its evaluations for one or more condition of use in any risk evaluation will vary as necessary to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment.* *(7) To the extent a determination as to the level of risk presented by a condition of use can be made, for example, using assumptions, uncertainty factors, and models or screening methodologies, EPA may determine that no further information or analysis is needed to complete its risk evaluation of the condition(s) of use.*

Supplemental Analysis

Charge Question 8.a: Please comment on whether the use of point of departure from analog data used in conjunction with the adjusted NIOSH-recommended exposure limit or the Occupational Safety and Health Administration (OSHA) standard for Particles Not Otherwise Regulated (PNOR) to develop an MOE provides utility in risk characterization concerning PV29. If not, please suggest alternative approaches or information that could be used to incorporate these values into the human health risk characterization.

Charge Question 8.b: Please comment on whether the screening-level estimate for the potential for lung overload with the NIOSH-recommended exposure limit or the Occupational Safety and Health Administration (OSHA) standard for Particles Not Otherwise Regulated (PNOR) and the predicted deposition fraction to the alveolar region predicted by the MPPD model (v3.04) from Orberdörster (1994), and whether this provides utility in risk characterization concerning PV29.

Oberdörster, G. (1994). Lung particle overload: implications for occupational exposures to particles. *Regulatory Toxicology and Pharmacology*, *21*(1), 123-135

#	Summary of Comments for Specific Issues Related to Charge Question 8	EPA/OPPT Response
EPA needs more current and/or accurate inhalation exposure data		
SACC	SACC COMMENTS: • Given that no acceptable inhalation toxicity studies are available for PV29, a properly designed inhalation study (*e.g.*, 28-day, aerosol, nose only, inhalable fraction with the high dose achieving toxicity which may be lung overload) would be needed to fill this data gap. • PV29 is assumed to not be bioavailable or readily absorbed by any applicable route of exposure since it may have poor water and lipid solubility. No absorption, distribution, metabolism, elimination (ADME)/toxicokinetic data were presented. However, mouse skin staining was observed after dosing by intra-peritoneal injection, gavage, and dermal application. The mechanism for this has not been ascertained. NAMs such as Organ on a Chip	EPA agrees that there are uncertainties inherent in making a determination about respiratory hazard without available inhalation toxicity data for C.I. Pigment Violet 29. However, as discussed in the final Risk Evaluation, with the new data obtained through the Section 4 test order to evaluate the solubility of C.I. Pigment Violet 29, EPA has a greater degree of confidence that it is poorly absorbed and therefore not metabolically active. Therefore, based on evidence that suggests chronic inhalation of such particles can trigger lung overload, EPA has determined that lung overload is the relevant effect for C.I. Pigment Violet 29 U.S. EPA (2019). As chronic inhalation data are available for Carbon Black, another pigment with low solubility and a similar particle diameter and relative density, EPA determined that these data are adequate to understand the potential hazards of

#	Summary of Comments for Specific Issues Related to Charge Question 8	EPA/OPPT Response
	(lung) or skin permeability in vitro assay should be considered. • Supplement available data by requesting personal monitoring data from the manufacturer which should include both respirable dust fraction and total dust.	chronic inhalation of C.I. Pigment Violet 29 and no additional inhalation toxicity data are needed. The staining effects are poorly explained in the assessments. However, with the submission of the new solubility data that confirms the low solubility of C.I. Pigment Violet 29 in water and octanol and as a result, the low potential for absorption, it is determined that these staining effects (which are inconsistently reported) are not representative of the chemical, but of issues with the way the studies are conducted. Regardless, these staining events did not result in adverse effects to the test organisms in the cases of oral and dermal exposure. EPA requested and received additional respirable dust monitoring data.
Supplemental inhalation analysis improves risk evaluation, but clarify sources of uncertainty		
73	PUBLIC COMMENTS: • EPA's updated inhalation risk characterization of PV29 provides additional rigor to the risk evaluation demonstrating low risk in occupational settings. EPA could, however, provide additional clarity by tabulating sources of uncertainty within the different MOE calculations. (73_1)	EPA has added language to the final Risk Evaluation to better describe the sources of uncertainty.
Supplemental inhalation analysis is inadequate		
55, 78, 82	PUBLIC COMMENTS: • The New Inhalation Analysis is inadequate to evaluate PV29's inhalation risks and rests upon	EPA agrees that the inhalation analysis presented in update to the Draft Risk Evaluation is inadequate based on data received to characterize the inhalation potential of PV29. EPA has updated the final Risk Evaluation to better explain the assumptions and modeling approach. EPA will be

#	Summary of Comments for Specific Issues Related to Charge Question 8	EPA/OPPT Response
	unsupported assumptions and an unvalidated, non-peer reviewed model. (78_5-11) • EPA assumes that Pigment Violet 29 is non-toxic and not absorbed via inhalation without providing adequate empirical data to support such assumptions and because of these major data gaps, EPA's new occupational inhalation analysis fails to demonstrate that PV29 is not risky. (82_1) • EPA's New Inhalation Analysis does not explain why EPA selected the screening-level lung overload calculation or discuss any uncertainties associated with the formula and its application to PV29. (55_2) • EPA's inhalation risk calculations based on the barium sulfate study are unsupported and underestimated. (78_13)	conducting an external peer review of Technical Support Documentation and User's Guide to accompany an EPA version (2020 v. 1.01) of the MPPD model for use in Agency assessments at the end of FY20. EPA acknowledges that the lack of inhalation toxicity data is an uncertainty. EPA is confident that, based on the physical chemical properties of the analogue Carbon Black, it is sufficiently similar to C.I. Pigment Violet 29 to be able to adequately describe the inhalation hazards of the chemical. EPA has updated the explanation of why it selected the screening-level lung overload calculation and has expanded the discussion of any uncertainties associated with this approach in the final Risk Evaluation. EPA has updated the inhalation approach in the final Risk Evaluation with an analogue that is more representative of the physical chemical properties of C.I. Pigment Violet 29.

Peer Review Comments on Whether or Not Information in the CBI Materials Was Accurately Reflected in the Publicly Available Summaries

Charge Question 9: Please comment on whether or not the information contained in the CBI materials provided to the panel is accurately reflected in the sanitized data that are made publicly available and robust summaries used in the risk evaluation for PV29.

#	Summary of Comments for Specific Issues Related to Charge Question 9	EPA/OPPT Response
Include justifications for redactions by companies		

#	Summary of Comments for Specific Issues Related to Charge Question 9	EPA/OPPT Response
SACC	SACC COMMENTS: • The Committee suggested EPA develop a protocol to include justifications [of redactions by companies] when providing the CBI materials.	For information reported to or otherwise obtained by EPA under TSCA, EPA currently requires CBI claims to be substantiated in accordance with TSCA sec. 14(c)(3) at the time the information is submitted, unless the information is exempt from upfront substantiation under TSCA sec. 14(c)(2). For information that is not reported to or otherwise obtained by EPA under TSCA, EPA requires CBI claims to be substantiated in accordance with the procedures set forth in 40 CFR Part 2, Subpart B.
Provide summaries of differences between full and redacted study reports		
SACC	SACC COMMENTS: • The Committee suggested providing, for each study involving CBI, a summary of the differences between the full study report and the redacted study report, with a focus on what information/data is critical to the assessment and how redactions could affect this information.	EPA acknowledges that this approach would be useful in future assessments where critical data are not publicly available as a result of CBI determinations. In the case of the data available for C.I. Pigment Violet 29, this is not necessary. Of the 24 studies initially claimed in full as CBI, 15 were released completely without redactions, and 8 study reports were released with partial redactions that do not affect the study details (redactions were only applied to the contact information of the laboratory staff and company). In the instance of the sub chronic toxicity study, the CBI claims were applied to the individual animal data tables and not the result summaries. Upon comparison of the fully unredacted and partially redacted study reports, EPA determined that the redactions did not apply to critical study details and therefore did not affect the ability of a reviewer to understand the results of the study. The study reports can be found in the docket for PV29 (EPA-HQ-OPPT-2018-0604).

#	Summary of Comments for Specific Issues Related to Charge Question 9	EPA/OPPT Response
Allow certain parties to examine full study reports		
SACC	SACC COMMENTS: • The Committee suggested that EPA come up with a means to allow certain parties to examine full (unredacted) studies.	EPA will explore this in cases where future assessments rely on information protected by CBI claims.

Other Peer Review Comments

Charge Question 10: Comments that do not fit into the other charge questions.

#	Summary of Comments for Specific Issues Related to Charge Question 10	EPA/OPPT Response
82	• The implementation of the Lautenberg Act has deviated dramatically from Congress' intent and the new law's requirements. (82_1)	EPA is committed to effectively implementing the Lautenberg Act's amendments to TSCA. EPA will incorporate meaningful and relevant feedback received during this public period into its future risk evaluations.

Cited References

Ankley, GT; Benoit, DA; Hoke, RA; Leonard, EN; West, CW; Phipps, GL; Mattson, VR; Anderson, LA. (1993). Development and evaluation of test methods for benthic invertebrates and sediments: Effects of flow rate and feeding on water quality and exposure conditions. Arch Environ Contam Toxicol 25: 12-19.

BASF. (1988). Testing the acute toxicity in the fish model Zebra danio (brachydanio rerio) over the course of 96 hours. Germany: Hoechst AG, Pharma Research Toxicology and Pathology.

BASF. (2012). H-28548: Paliogen violet 5011, Daphnia magna, acute immobilization test. Pszczyna, Poland: Institute of Industrial Organic Chemistry, Branch Pszcyna Department of Ecotoxicology.

Cherrie, JW; Semple, S; Christopher, Y; Saleem, A; Hughson, GW; Philips, A. (2006). How important is inadvertent ingestion of hazardous substances at work? Ann Occup Hyg 50: 693-704.

Elder, A; Gelein, R; Finkelstein, JN; Driscoll, KE; Harkema, J; Oberdorster, G. (2005). Effects of subchronically inhaled carbon black in three species I Retention kinetics, lung inflammation, and histopathology. Toxicol Sci 88: 614-629. http://dx.doi.org/10.1093/toxsci/kfi327.

Mackay, D; Di Guardo, A; Paterson, S; Cowan, CE. (1996). Evaluating the environmental fate of a variety of types of chemicals using the EQC model. Environ Toxicol Chem 15: 1627-1637.

Nicolaou, C. (2020). Determination of the Solubility of C.I. PV29 in 1-Octanol and Water. Colors Technology Analytical Laboratory. https://beta.regulations.gov/document/EPA-HQ-OPPT-2020-0070-0008.

U.S. EPA. (2017). Scope of the risk evaluation for Pigment Violet 29 (Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone): CASRN: 81-33-4 [EPA Report]. (740-R1-7011). U.S. EPA, Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics. https://www.epa.gov/sites/production/files/2017-06/documents/pv29_scope_06-22-17.pdf.

U.S. EPA. (2018a). Application of systematic review in TSCA risk evaluations. (740-P1-8001). Washington, DC: U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf.

U.S. EPA. (2018b). Draft Risk Evaluation for C.I. Pigment Violet 29.

U.S. EPA. (2019). U.S. EPA Integrated Science Assessment for particulate matter [EPA Report]. (EPA/600/R-19/188). https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=347534.

U.S. EPA. (2020a). Final Risk Evaluation for C.I. Pigment Violet 29, Supplemental File: Information Received from Manufacturing Stakeholders.

U.S. EPA. (2020b). Final Risk Evaluation for C.I. Pigment Violet 29, Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies.

U.S. EPA. (2020c). Final Risk Evaluation for C.I. Pigment Violet 29, Systematic Review Supplemental File: Data Quality Evaluation of Physical-Chemical Property Studies.