

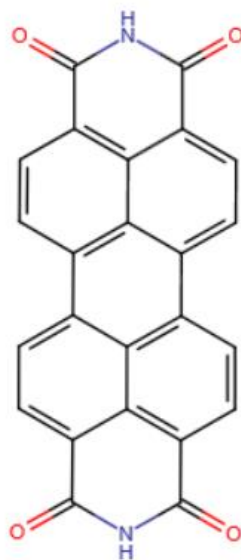


**Revised Draft Risk Evaluation for
C.I. Pigment Violet 29
(Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-
1,3,8,10(2H,9H)-tetrone)**

Systematic Review Supplemental File:

Data Quality Evaluation of Human Health Hazard Studies

CASRN: 81-33-4



October 2020

This document is a compilation of tables for the data extraction and evaluation for C.I. Pigment Violet 29 (CASRN 81-33-4). Each table shows the data point or set or information element that was extracted and evaluated from a data source in accordance with Appendix D of the *Application of Systematic Review in TSCA Risk Evaluations* [U.S. EPA \(2018\)](#). If the source contains more than one data set or information element, the review provides an overall confidence score for each data set or information element that is found in the source. Therefore, it is possible that a source may have more than one overall quality/confidence score.

Table of Contents

Table 1. Acute Oral Toxicity Study with Rats, BASF (1975b).....	3
Table 2. Acute Oral Toxicity Study with Rats, BASF (1978d).....	7
Table 3. Acute Oral Toxicity Study with Rats, Rupprich and Weigand (1984c).....	11
Table 4. Acute Inhalation Toxicity Study with Rats, BASF (1975a).....	14
Table 5. Acute Inhalation Toxicity Study with Rats, BASF (1978b).....	21
Table 6. Acute Intraperitoneal Toxicity Study with Mice, BASF (1975e)	27
Table 7. Acute Intraperitoneal Toxicity Study with Mice, BASF (1978c)	31
Table 8. Reproduction/Developmental Toxicity Screening Test with Rats, Stark et al. (2013).....	35
Table 9. Acute Dermal Irritation Study, BASF (1975d)	38
Table 10. Acute Dermal Irritation Study, BASF (1978e).....	42
Table 11. Acute Dermal Irritation Study, Rupprich and Weigand (1984a).....	46
Table 12. Eye Irritation Study, BASF (1975c).....	49
Table 13. Eye Irritation Study, BASF (1978a).....	53
Table 14. Eye Irritation Study, Rupprich and Weigand (1984b).....	57
Table 15. Local Lymph Node Assay, Johnson (1999)	60
Table 16. Study of the Mutagenic Potential in Strains of Salmonella typhimurium (AMES Test) and Escherichia coli, Jung and Weigand (1983)	64
Table 17. Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro, Wollny (2012)	68
Table 18. Effects of Subchronically Inhaled Carbon Black, Elder et al. (2005)	72

Table 1. Acute Oral Toxicity Study with Rats, [BASF \(1975b\)](#)

Study Reference:	BASF. 1975. Acute oral toxicity with rats. BASF Report XXV/454. Product Safety Basel, BASF Schweiz AG, Switzerland.[as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731529.					
Note:	Study guideline was not indicated in the study report					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASRN number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was not described but it is inferred to be solid state based on the physical/chemical properties of PV29.	2	2	4
	2. Test substance source	Low	No details were provided about the source and lot number of the test substance.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	Low	A concurrent negative control group was not reported. It is inferred that the laboratory did not include the negative control because water (vehicle) would not be triggering a response.	3	2	6
	5. Positive controls	Not rated	Not rated/applicable - Positive controls are not necessary for this study type.	NR	NR	NR
	6. Randomized allocation	Low	The study report did not state how animals were	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			allocated to study groups.			
Exposure characterization	7. Preparation and storage of test substance	Low	Test substance is likely poorly soluble in water based on the physicochemical properties of the CASRN. The study report states that the test substance was prepared as a 50% aqueous suspension in water; however, no details were provided on test substance preparation (<i>e.g.</i> , stirring, and whether homogenous when administered) and it is not evident that the aqueous suspension was homogenous when dosing was performed.	3	1	3
	8. Consistency of Exposure administration	Low	Details of exposure administration were not fully addressed. The study report states that a single dose was administered via gavage to each animal; however, the dosing volume was not reported so it is not evident that exposure administration was the same for all animals.	3	1	3
	9. Reporting of doses / concentrations	High ^A		1	2	2
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High ^A		1	1	1

REVISED DRAFT – DO NOT CITE OR QUOTE

	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	Medium	Health status and age at initiation were not reported.	2	2	4
	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3
	15. Number per group	High ^A		1	1	1
Outcome Assessment	16. Outcome assessment methodology	Medium	Study generally describes that investigators observed mortality and clinical signs at various timepoints during the 14-day observation period. However, details on how those observations were collected were not provided.	2	2	4
	17. Consistency of outcome assessment	Medium	It is inferred that the investigators used the same outcome assessment method for the treated animals based on details provided in the study. However, the study did not address the measures that the investigators put in place to have consistency in the outcome assessment.	2	1	2
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies	NR	NR	NR
	20. Negative Control Response	Not rated	Not rated/applicable - A negative control group was not included.	NR	NR	NR
Confounding/variable control	21. Confounding	Medium	Lack of reporting of food/water intake	2	2	4

REVISED DRAFT – DO NOT CITE OR QUOTE

	variables in test setup and procedures					
	22. Outcomes unrelated to exposure	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	1	3
Data presentation and analysis	23. Statistical methods	Not rated	Reviewer implied that the investigators did not conduct a statistical analysis.	NR	NR	NR
	24. Reporting of data	Medium	Outcome data were provided. It would have been helpful to have outcome data for the vehicle control.	2	2	4
			Sum of scores:	42	27	56
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	2.074	Overall Score (Rounded):	2.1
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			Medium
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 2. Acute Oral Toxicity Study with Rats, [BASF \(1978d\)](#)

Study Reference:	BASF. 1978. Study report for CAS 81-33-4, Acute oral toxicity with rats. BASF Report 77/360. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731530.					
Note:	Study guideline was not indicated in the study report					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASRN number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was not described but it is inferred to be solid state based on the physical/chemical properties of PV29.	2	2	4
	2. Test substance source	Low	No details were provided about the source and lot number of the test substance.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	Low	A concurrent negative control group was not reported. It is inferred that the laboratory did not include the negative control because water (vehicle) would not be triggering a response.	3	2	6
	5. Positive controls	Not rated	Not rated/applicable - Positive controls are not necessary for this study type.	NR	NR	NR
	6. Randomized allocation	Low	The study report did not state how animals were allocated to study groups.	3	1	3
Exposure characterization	7. Preparation and storage of test substance	Low	Test substance preparation was not fully reported. The vehicle (0.5% aqueous solution of carboxymethylcellulose, 50% suspension with test	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			item) was stated, but methods of preparation (<i>e.g.</i> , whether methods ensured that test item suspension was homogenous) and storage were not addressed.			
	8. Consistency of Exposure administration	Low	Details of exposure administration were not fully reported. The study report states that the test substance was administered as a single gavage application to each animal, but the dosing volume was not reported so it is not evident that exposure administration was the same for all animals.	3	1	3
	9. Reporting of doses / concentrations	High ^A		1	2	2
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High ^A		1	1	1
	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	Medium	Health status and age at initiation were not reported.	2	2	4
	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

	15. Number per group	High		1	1	1
Outcome Assessment	16. Outcome assessment methodolo gy	Medium	Study generally describes that investigators observed mortality and clinical signs at various timepoints during the 14-day observation period. However, details on how those observations were collected were not provided.	2	2	4
	17. Consistenc y of outcome assessment	Medium	It is inferred that the investigators used the same outcome assessment method for the treated animals based on details provided in the study. However, the study did not address the measures that the investigators put in place to have consistency in the outcome assessment.	2	1	2
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies.	NR	NR	NR
	20. Negative Control Response	Not rated	Not rated/applicable - A negative control group was not included.	NR	NR	NR
	Confounding/ variable control	21. Confoundi ng variables in test setup and procedures	Medium	Lack of reporting of food/water intake and respiratory rate	2	2
22. Outcomes unrelated to exposure		Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	1	3
Data presentation and analysis	23. Statistical methods	Not rated	Reviewer implied that the investigators did not conduct a statistical analysis.	NR	NR	NR

REVISED DRAFT – DO NOT CITE OR QUOTE

	24. Reporting of data	Medium	Outcome data were provided. It would have been helpful to have outcome data for the vehicle control.	2	2	4
			Sum of scores:	42	27	56
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	2.074	Overall Score (Rounded):	2.1
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			Medium
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 3. Acute Oral Toxicity Study with Rats, [Rupprich and Weigand \(1984c\)](#)

Study Reference:	Rupprich, N, Weigand, W. 1984. Testing the acute oral toxicity in the male and female Wistar rat. Hoechst, Pharma Research Toxicology. Report No. 84.0225. Report date: May 2, 1984. HERO ID: 4731531.					
Note:	Study guideline was not indicated in the study report					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	High	The test substance was identified definitively and the specific form was characterized	1	2	2
	2. Test substance source	Medium	Source was incompletely reported.	2	1	2
	3. Test substance purity	Medium	Product contained 80% active ingredient (Perylimid); other components were reported as 10% KOH, 8% diverse organic contaminations, which were not identified, approx 1% inorganic salts, and approx 1% water.	2	1	2
Test setup	4. Negative controls	Not rated	A concurrent negative control group is not required for this study type.	NR	NR	NR
	5. Positive controls	Not rated	A concurrent positive control group is not required for this study type.	NR	NR	NR
	6. Randomized allocation	Low	The study did not report how animals were allocated to study groups.	3	1	3
Exposure characterization	7. Preparation and storage of test substance	Low	The study report states that the test substance was prepared as a suspension in the	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			carrier, 2% starch sludge, but no further details on preparation (<i>e.g.</i> , homogeneity of suspension, solubility in starch sludge) or storage of the test substance were reported.			
	8. Consistency of Exposure administration	Medium	Consistent dosing volume was reported but, the study report does not specifically state that exposures were otherwise administered consistently (<i>e.g.</i> , at the same time of day).	2	1	2
	9. Reporting of doses / concentrations	High ^A		1	2	2
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High ^A		1	1	1
	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	Medium	Health status and age at initiation were not reported.	2	2	4
	14. Adequacy and consistency of animal husbandry conditions	High ^A		1	1	1
	15. Number per group	High ^A		1	1	1
Outcome Assessment	16. Outcome assessment methodology	High ^A		1	2	2
	17. Consistency of outcome assessment	High ^A		1	1	1

REVISED DRAFT – DO NOT CITE OR QUOTE

	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies.	NR	NR	NR
	20. Negative Control Response	Not rated	A negative control group was not included.	NR	NR	NR
Confounding/ variable control	21. Confounding variables in test setup and procedures	Medium	Lack of reporting of food/water intake and respiratory rate	2	2	4
	22. Outcomes unrelated to exposure	High ^A		1	1	1
Data presentation and analysis	23. Statistical methods	High	The data was provided, but statistical analysis is not required	1	1	1
	24. Reporting of data	High ^A		1	2	2
			Sum of scores:	29	26	37
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.423	Overall Score (Rounded):	1.4
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	Overall Quality Level:			HIGH
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 4. Acute Inhalation Toxicity Study with Rats, [BASF \(1975a\)](#)

Study Reference:	BASF. 1975. Acute inhalation toxicity with rats. BASF Report XXV/454. Product Safety Basel, BASF Schweiz AG, Switzerland. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID 4731525.					
Note:	Study report indicated that this study was not conducted according to a test guideline					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASR number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was ambiguously characterized mentioning both vapors and dust.	2	2	4
	2. Test substance source	Low	No details were provided about the test substance source.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	Medium	The study did not use a vehicle control. The study used a concurrent air control.	2	2	4
	5. Positive controls	Not rated	A positive control is not necessary for this study.	NR	NR	NR
	6. Randomized allocation	Low	The study did not provide details on the randomized	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			allocation of animals.			
Exposure characterization	7. Preparation and storage of test substance	Low	The study did not discuss details about the preparation and/or storage conditions of the test substance. These details are important to determine if the animals were properly exposed to a well-characterized test substance under carefully controlled conditions.	3	1	3
	8. Consistency of Exposure administration	Unacceptable	Reviewer cannot determine whether consistency of exposure was achieved due to lack of analytical method to measure exposure in the chamber (<i>e.g.</i> , only nominal concentrations were reported).	4	1	4
	9. Reporting of doses / concentrations	Unacceptable	Nominal but not actual concentrations were reported. Nominal concentrations are usually quite close to actual concentrations for gases, but they can be much greater for vapor and aerosols. This creates a major uncertainty in the study.	4	2	8

REVISED DRAFT – DO NOT CITE OR QUOTE

	10. Exposure frequency and duration	Low	Rats were exposed in an atmosphere saturated with vapors for 8 hrs. The exposure duration is not typical for an acute inhalation study and this was not explained.	3	1	3
	11. Number of exposure groups and dose spacing	Low	Air control and one exposure concentration were conducted. The objective of the test was not described which would have helped to understand if a single test concentration or multiple concentrations would be appropriate.	3	1	3
	12. Exposure route and method	Unacceptable	The study aimed at investigating animal toxicity to an atmosphere saturated with vapors of the volatile component of PV29. Since the study said that dust is expected by inhalation, this is an inappropriate exposure method. Further, specific details were missing such as the equipment and method used to generate the	4	1	4

REVISED DRAFT – DO NOT CITE OR QUOTE

			chamber atmosphere, description of the inhalation chamber, failure to use an analytical method to analyze the test atmosphere concentrations. Also, the authors admitted the limitations of the study by indicating that “the inhalation hazard test is insufficient for non-volatile substances”.			
Test organisms	13. Test animal characteristics	Low	Study provided minimal information on the test animal characteristics (e.g., strain, health status, age).	3	2	6
	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3
	15. Number per group	Medium	Number of animals per treatment group/sex was considered adequate for an acute inhalation study. There were observed variations in the number of animals for air control groups (3 rats/sex) and treatment group (6 rats/sex), but no explanation was offered to	2	1	2

REVISED DRAFT – DO NOT CITE OR QUOTE

			account for the difference.			
Outcome Assessment	16. Outcome assessment methodology	Low	Significant deficiencies in the reported outcome assessment methodology (<i>i.e.</i> , limited information available).	3	2	6
	17. Consistency of outcome assessment	Low	Details regarding the execution of the study protocol for outcome assessment (<i>e.g.</i> , timing of assessment across groups) were not discussed.	3	1	3
	18. Sampling adequacy	Medium	Details regarding sampling of outcomes were not reported. Mortality incidence was recorded in the data table at five exposure times (3 min, 10 min, 1 hr, 3 hrs and 8 hrs). The reviewer implied that the investigators assessed mortality and clinical signs frequently during the 8-hr exposure, but this was not explicitly explained in the report. Rats were observed for 7 days after cessation of exposure.	2	1	2

REVISED DRAFT – DO NOT CITE OR QUOTE

	19. Blinding of assessors	Not rated	Blinding is not typically done for acute inhalation studies that are assessing mortality, clinical signs (e.g., irritation) and gross pathology.	NR	NR	NR
	20. Negative Control Response	Low	The biological responses of the negative control group(s) were reported, but the responses for the negative controls have high uncertainties due to the exposure characterization issues in the study.	3	1	3
Confounding/ variable control	21. Confounding variables in test setup and procedures	Low	Although initial body weight was reported, the post-treatment body weights were not reported to confirm the study's claim that the treatment did not affect body weight. It is not possible to determine if there were confounding variables with the limited information given in the report.	3	2	6
	22. Outcomes unrelated to exposure	Low	It is not possible to determine whether health outcomes unrelated to exposure	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			affected reported outcomes given the limited information in the report.			
Data presentation and analysis	23. Statistical methods	Not rated	Reviewer implied that the investigators did not conduct a statistical analysis because it was not necessary (e.g., one control group, one treatment group, no effects observed).	NR	NR	NR
	24. Reporting of data	Low	Outcome data were minimally provided and discussed.	3	2	6
			Sum of scores:		28	82
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	2.929	Overall Score (Rounded):	2.9¹
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	Overall Quality Level:			Unacceptable¹
Footnote 1: Consistent with our Application of Systematic Review in TSCA Risk Evaluations document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, three of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.						

Table 5. Acute Inhalation Toxicity Study with Rats, [BASF \(1978b\)](#)

Study Reference:	BASF. 1978. Study report for CAS 81-33-4, Acute inhalation toxicity with rats. BASF Report 77/360. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731526.					
Note:	Study report indicated that this study was not conducted according to a test guideline					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASR number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was ambiguously characterized mentioning both vapors and dust.	2	2	4
	2. Test substance source	Low	No details were provided about the test substance source.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	Unacceptable	The study did not use a vehicle control. The study used a concurrent air control.	4	2	8
	5. Positive controls	Not rated	A positive control is not necessary for this study.	NR	NR	NR
	6. Randomized allocation	Low	The study did not provide details on the randomized allocation of animals.	3	1	3
Exposure characterization	7. Preparation and storage of test substance	Low	The study did not discuss details about the preparation and/or storage conditions of the test substance. These	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			details are important to determine if the animals were properly exposed to a well-characterized test substance under carefully controlled conditions.			
8. Consistency of Exposure administration	Unacceptable		Reviewer cannot determine whether consistency of exposure was achieved due to lack of analytical method to measure exposure in the chamber (<i>e.g.</i> , only nominal concentrations were reported).	4	1	4
9. Reporting of doses / concentrations	Unacceptable		Nominal but not actual concentrations were reported. Nominal concentrations are usually quite close to actual concentrations for gases, but they can be much greater for vapor and aerosols. This creates a major uncertainty in the study.	4	2	8
10. Exposure frequency and duration	Low		Rats were exposed in an atmosphere saturated with vapors for 7 hrs. The exposure duration is not typical for an acute inhalation study and this was not explained.	3	1	3
11. Number of exposure groups and dose spacing	Low		Study included one exposure concentration but no mention about the air control groups. The	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			objective of the test was not described which would have helped to understand if a single test concentration or multiple concentrations would be appropriate.			
	12. Exposure route and method	Unacceptable	The study aimed at investigating animal toxicity to an atmosphere saturated with vapors of the volatile component of PV29. Since the study said that dust is expected by inhalation, this is an inappropriate exposure method. Further, specific details were missing such as the equipment and method used to generate the chamber atmosphere, description of the inhalation chamber, failure to use an analytical method to analyze the test atmosphere concentrations. Also, the authors admitted the limitations of the study by indicating that “the inhalation hazard test is insufficient for non-volatile substances”.	4	1	4
Test organisms	13. Test animal characteristics	Low	Study provided minimal information on the test animal characteristics	3	2	6

REVISED DRAFT – DO NOT CITE OR QUOTE

			(e.g., strain, health status, age).			
	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3
	15. Number per group	Low	Number of animals per treatment group/sex was considered adequate for an acute inhalation study. Report did not report the number of animals for air control groups. Reviewer assumed that the investigators might have used the air control groups from the previous 8-hr acute inhalation toxicity study.	3	1	3
Outcome Assessment	16. Outcome assessment methodology	Low	Significant deficiencies in the reported outcome assessment methodology (<i>i.e.</i> , limited information available).	3	2	6
	17. Consistency of outcome assessment	Low	Details regarding the execution of the study protocol for outcome assessment (<i>e.g.</i> , timing of assessment across groups) were not discussed.	3	1	3
	18. Sampling adequacy	Medium	Details regarding sampling of outcomes were not reported. Mortality incidence was recorded in the data table at five exposure times (3 min, 10 min, 1 hr, 3 hrs and 7 hrs).	2	1	2

REVISED DRAFT – DO NOT CITE OR QUOTE

			The reviewer implied that the investigators assessed mortality and clinical signs frequently during the 8-hr exposure, but this was not explicitly explained in the report. Rats were observed for 7 days after cessation of exposure.			
	19. Blinding of assessors	Not rated	Blinding is not typically done for acute inhalation studies that are assessing mortality, clinical signs (<i>e.g.</i> , irritation) and gross pathology.	NR	NR	NR
	20. Negative Control Response	Unacceptable	The biological responses of the negative control group(s) were not addressed in the study.	4	1	4
Confounding/ variable control	21. Confounding variables in test setup and procedures	Low	Although initial body weight was reported, the post-treatment body weights were not reported to confirm the study's claim that the treatment did not affect body weight. It is not possible to determine if there were confounding variables with the limited information given in the report.	3	2	6
	22. Outcomes unrelated to exposure	Low	It is not possible to determine whether health outcomes unrelated to exposure affected reported outcomes given the limited	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			information in the report.			
Data presentation and analysis	23. Statistical methods	Not rated	Reviewer implied that the investigators did not conduct a statistical analysis because it was not necessary (<i>e.g.</i> , one control group, one treatment group, no effects observed).	NR	NR	NR
	24. Reporting of data	Unacceptable	Data presentation was inadequate (<i>e.g.</i> , the report does not differentiate among findings between air control and treatment groups).	4	2	8
			Sum of scores:		28	90
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	3.214	Overall Score (Rounded):	3.2¹
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	Overall Quality Level:			Unacceptable¹
Footnote 1: Consistent with our Application of Systematic Review in TSCA Risk Evaluations document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, seven of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.						

Table 6. Acute Intraperitoneal Toxicity Study with Mice, [BASF \(1975e\)](#)

Study Reference:	BASF. 1975. Summary of toxicological investigations with CAS 81-33-4, Acute intraperitoneal toxicity with mice. BASF Report XXV/454. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731527.					
Note:	Study report indicated that this study was not conducted according to a test guideline but was conducted according to an internal protocol.					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASRN number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was not described but it is inferred to be solid state based on the physical/chemical properties of PV29.	2	2	4
	2. Test substance source	Low	No details were provided about the source and lot number of the test substance.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	Low	A concurrent negative control group was not reported. It is inferred that the laboratory had historical data testing mice with carboxymethyl cellulose (vehicle) and showing no mortality. Carboxymethyl cellulose is non-toxic.	3	2	6
	5. Positive controls	Not rated	Not rated/applicable - A concurrent positive control group is not required for this study type.	NR	NR	NR

REVISED DRAFT – DO NOT CITE OR QUOTE

	6. Randomized allocation	Low	The study report did not state how animals were allocated to study groups.	3	1	3
Exposure characterization	7. Preparation and storage of test substance	Low	Test substance preparation was not fully reported. The vehicle (0.5% aqueous carboxymethyl cellulose, 21.5%, 46.4% or 50% aqueous suspension) was stated, but the methods of preparation (<i>e.g.</i> , whether methods ensured that test item suspension was homogenous) and storage were not addressed.	3	1	3
	8. Consistency of Exposure administration	Low	Details of exposure administration were not fully reported. The study report states that the test substance was administered as a single intraperitoneal application but the volume administered was not reported.	3	1	3
	9. Reporting of doses / concentrations	High ^A		1	2	2
	10. Exposure frequency and duration	High	Single I.P injection	1	1	1
	11. Number of exposure groups and dose spacing	High	3 exposure groups	1	1	1
	12. Exposure route and method	High ^A		1	1	1
	Test organisms	13. Test animal characteristics	Low	Study provided minimal information on the test animal characteristics (<i>e.g.</i> , strain, health status, age).	3	2

REVISED DRAFT – DO NOT CITE OR QUOTE

	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3
	15. Number per group	High	5 animals per sex per exposure group	1	1	1
Outcome Assessment	16. Outcome assessment methodology	Medium	Study generally describes that investigators observed mortality and clinical signs at various timepoints during the 14-day observation period. However, details on how those observations were collected were not provided.	2	2	4
	17. Consistency of outcome assessment	Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were not reported, and these deficiencies are likely to have a substantial impact on results.	3	1	3
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies.	NR	NR	NR
	20. Negative Control Response	Not rated	Not rated/applicable - A negative control group was not included.	NR	NR	NR
Confounding/variable control	21. Confounding variables in test setup and procedures	Low	Although initial body weight was reported, the post-treatment body weights were not reported to confirm the study's claim that the treatment did not affect body weight. It is not possible to determine if there were	3	2	6

REVISED DRAFT – DO NOT CITE OR QUOTE

			confounding variables with the limited information given in the report.			
	22. Outcomes unrelated to exposure	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	1	3
Data presentation and analysis	23. Statistical methods	Not rated	Reviewer implied that the investigators did not conduct a statistical analysis.	NR	NR	NR
	24. Reporting of data	Low	Outcome data were minimally provided and discussed.	3	2	6
			Overall Score:	46	27	63
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	2.333	Overall Score (Rounded):	2.3
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			Low
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 7. Acute Intraperitoneal Toxicity Study with Mice, [BASF \(1978c\)](#)

Study Reference:	BASF. 1978. Study report for CAS 81-33-4, Acute intraperitoneal toxicity with mice. BASF Report 77/360. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731528.					
Note:	Study report indicated that this study was not conducted according to a test guideline but was conducted according to an internal protocol.					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASRN number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was not described but it is inferred to be solid state based on the physical/chemical properties of PV29.	2	2	4
	2. Test substance source	Low	No details were provided about the source and lot number of the test substance.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	Low	A concurrent negative control group was not reported. It is inferred that the laboratory had historical data testing mice with carboxymethyl cellulose (vehicle) and showing no mortality. Carboxymethyl cellulose is non-toxic.	3	2	6
	5. Positive controls	Not rated	Not rated/applicable - A concurrent positive control group is not required for this study type.	NR	NR	NR

REVISED DRAFT – DO NOT CITE OR QUOTE

	6. Randomized allocation	Low	The study report did not state how animals were allocated to study groups.	3	1	3
Exposure characterization	7. Preparation and storage of test substance	Low	Test substance preparation was not fully reported. The vehicle (0.5% aqueous carboxymethyl cellulose, 46.4% or 50% aqueous suspension) was stated, but the methods of preparation (<i>e.g.</i> , whether methods ensured that test item suspension was homogenous) and storage were not addressed.	3	1	3
	8. Consistency of Exposure administration	Low	Details of exposure administration were not fully reported. The study report states that the test substance was administered as a single intraperitoneal application but the volume administered was not reported.	3	1	3
	9. Reporting of doses / concentrations	High ^A		1	2	2
	10. Exposure frequency and duration	High	Single I.P injection	1	1	1
	11. Number of exposure groups and dose spacing	High	3 exposure groups	1	1	1
	12. Exposure route and method	High ^A		1	1	1
	Test organisms	13. Test animal characteristics	Low	Study provided minimal information on the test animal characteristics (<i>e.g.</i> , strain, health status, age).	3	2

REVISED DRAFT – DO NOT CITE OR QUOTE

	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3
	15. Number per group	High	5 animals per sex per exposure group	1	1	1
Outcome Assessment	16. Outcome assessment methodology	Medium	Study generally describes that investigators observed mortality and clinical signs at various timepoints during the 14-day observation period. However, details on how those observations were collected were not provided.	2	2	4
	17. Consistency of outcome assessment	Low	Details regarding the execution of the study protocol for outcome assessment (<i>e.g.</i> , timing of assessment across groups) were not reported, and these deficiencies are likely to have a substantial impact on results.	3	1	3
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies.	NR	NR	NR
	20. Negative Control Response	Not rated	Not rated/applicable - A negative control group was not included.	NR	NR	NR
Confounding/variable control	21. Confounding variables in test setup and procedures	Low	Although initial body weight was reported, the post-treatment body weights were not reported to confirm the study's claim that the treatment did not affect body weight. It is not possible to determine if there were confounding	3	2	6

REVISED DRAFT – DO NOT CITE OR QUOTE

			variables with the limited information given in the report.			
	22. Outcomes unrelated to exposure	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	1	3
Data presentation and analysis	23. Statistical methods	Not rated	Reviewer implied that the investigators did not conduct a statistical analysis.	NR	NR	NR
	24. Reporting of data	Medium	Outcome data were provided. It would have been helpful to have outcome data for the vehicle control.	2	2	4
			Overall Score:	45	27	61
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	2.259	Overall Score (Rounded):	2.3
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			Low
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 8. Reproduction/Developmental Toxicity Screening Test with Rats, [Stark et al. \(2013\)](#)

Study Reference:	Stark, D., Treumann, S., van Ravenzwaay, B. 2013. Reproduction/developmental Toxicity Screening Test with Wistar Rats Oral Administration (Gavage). BASF SE, Germany. Project No. 80R0223/11C162. For BASF SE, Germany. HERO ID: 4731538.					
Note:	Study report indicates the study was conducted according to OECD TG 421 and OPPTS 870.3550					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	High	The test substance was identified definitively and detailed analysis of the characterization including a description of the form was provided.	1	2	2
	2. Test substance source	High	Test item was received by the submitter and the batch number was provided.	1	1	1
	3. Test substance purity	High	Purity was characterized in the appendix of the study.	1	1	1
Test setup	4. Negative controls	High ^A		1	2	2
	5. Positive controls	Not rated	No positive controls were needed for this study.	NR	NR	NR
	6. Randomized allocation	Medium	Animals were distributed according to weight so that weight variations did not exceed 20% of the mean weight of each sex.	2	1	2
Exposure characterization	7. Preparation and storage of test substance	High ^A		1	1	1
	8. Consistency of Exposure administration	High ^A		1	1	1
	9. Reporting of doses / concentrations	High ^A		1	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High ^A		1	1	1
	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	High ^A		1	2	2
	14. Adequacy and consistency of animal husbandry conditions	High ^A		1	1	1
	15. Number per group	High ^A		1	1	1
Outcome Assessment	16. Outcome assessment methodology	High ^A		1	2	2
	17. Consistency of outcome assessment	High ^A		1	1	1
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	Initial histopathology review was the only subjective assessment conducted, and this metric is not applicable.	NR	NR	NR
	20. Negative Control Response	High ^A		1	1	1
Confounding/variable control	21. Confounding variables in test setup and procedures	High ^A		1	2	2
	22. Outcomes unrelated to exposure	High ^A		1	1	1

REVISED DRAFT – DO NOT CITE OR QUOTE

Data presentation and analysis	23. Statistical methods	High ^A		1	1	1
	24. Reporting of data	High ^A		1	2	2
			Sum of scores:	23	29	30
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.034	Overall Score (Rounded):	1.0
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	Overall Quality Level:			HIGH
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 9. Acute Dermal Irritation Study, [BASF \(1975d\)](#)

Study Reference:	BASF. 1975. Skin irritation study. BASF Report XXV/454. Product Safety Basel, BASF Schweiz AG, Switzerland. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731532.					
Note:	Study guideline was not indicated in the study report					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASRN number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was not described but it is inferred to be solid state based on the physical/chemical properties of PV29.	2	2	4
	2. Test substance source	Low	No details were provided about the source and lot number of the test substance.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	Medium	Use of a negative control was not reported, but this is not considered to have a substantial impact on results since untreated skin usually serves as the negative control in this type of study.	2	2	4
	5. Positive controls	Not rated	Positive controls are typically not necessary for this study type.	NR	NR	NR

REVISED DRAFT – DO NOT CITE OR QUOTE

	6. Randomized allocation	Not rated	Only two individual animals were tested, so randomization was not required.	NR	NR	NR
Exposure characterization	7. Preparation and storage of test substance	Low	The study report states that the test substance was prepared as a 50% aqueous suspension in water; however, no details were provided on test substance preparation (<i>e.g.</i> , stirring, and whether homogenous when applied).	3	1	3
	8. Consistency of Exposure administration	Low	Few details were provided on application of the test substance to skin so it is not clear that exposures were consistent.	3	1	3
	9. Reporting of doses / concentrations	Low	Study report states that test substance was given as a 50% aqueous suspension, but no details are provided on the actual amount (<i>e.g.</i> , grams) of test substance administered in the application.	3	2	6
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High ^A		1	1	1
	12. Exposure route and method	High ^A		1	1	1
	Test organisms	13. Test animal characteristics	Medium	Health status and age at initiation of treatment were not reported.	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3
	15. Number per group	Low	Only two animals were treated.	3	1	3
Outcome Assessment	16. Outcome assessment methodology	Low	Significant deficiencies in the reported outcome assessment methodology (<i>i.e.</i> , limited information).	3	2	6
	17. Consistency of outcome assessment	High ^A		1	1	1
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies. Note that the grading of dermal responses is subjective. Training in observing the dermal responses and translating them to a score promotes harmonization of subjective results.	NR	NR	NR
	20. Negative Control Response	Not rated	Negative controls were not required for the study.	NR	NR	NR
Confounding/variable control	21. Confounding variables in test setup and procedures	Medium	Initial food/water intake were not reported but this is not likely to have a significant impact on results.	2	2	4
	22. Outcomes unrelated to exposure	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

Data presentation and analysis	23. Statistical methods	Not rated	Reviewer implied that the investigators did not conduct a statistical analysis.	NR	NR	NR
	24. Reporting of data	High	Dermal responses were reported for both female rabbits at different timepoints.	1	2	2
			Sum of scores:	41	26	56
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	2.154	Overall Score (Rounded):	2.2
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			Medium
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 10. Acute Dermal Irritation Study, [BASF \(1978e\)](#)

Study Reference:	BASF. 1978. Study report for CAS 81-33-4, Skin irritation study. BASF Report 77/360. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731533.					
Note:	Study report did not indicate whether a test guideline was followed.					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASRN number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was not described but it is inferred to be solid state based on the physical/chemical properties of PV29.	2	2	4
	2. Test substance source	Low	No details were provided about the source and lot number of the test substance.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	Medium	Use of a negative control was not reported, but this is not considered to have a substantial impact on results since untreated skin usually serves as the negative control in this type of study.	2	2	4
	5. Positive controls	Not rated	Positive controls are typically not necessary for this study type.	NR	NR	NR
	6. Randomized allocation	Not rated	Only two individual animals were tested, so	NR	NR	NR

REVISED DRAFT – DO NOT CITE OR QUOTE

			randomization was not required.			
Exposure characterization	7. Preparation and storage of test substance	Low	The study report states that the test substance was prepared as a 50% aqueous suspension in water; however, no details were provided on test substance preparation (<i>e.g.</i> , stirring, and whether homogenous when applied).	3	1	3
	8. Consistency of Exposure administration	Low	Few details were provided on application of the test substance to skin so it is not clear that exposures were consistent.	3	1	3
	9. Reporting of doses / concentrations	Low	Study report states that test substance was given as a 50% aqueous suspension, but no details are provided on the actual amount (<i>e.g.</i> , grams) of test substance administered in the application.	3	2	6
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High ^A		1	1	1
	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	High	Health status and age at initiation of treatment were not reported.	1	2	2
	14. Adequacy and consistency of animal	Medium	Study provided minimal information on the adequacy of animal	2	1	2

REVISED DRAFT – DO NOT CITE OR QUOTE

	husbandry conditions		husbandry conditions.			
	15. Number per group	Low	Only three animals were treated.	3	1	3
Outcome Assessment	16. Outcome assessment methodology	Low	Significant deficiencies in the reported outcome assessment methodology (<i>i.e.</i> , limited information).	3	2	6
	17. Consistency of outcome assessment	High ^A		1	1	1
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically done. Note that the grading of dermal responses is subjective. Training in observing the dermal responses and translating them to a score promotes harmonization of subjective results.	NR	NR	NR
	20. Negative Control Response	Not rated	Negative controls were not required for the study.	NR	NR	NR
Confounding/variable control	21. Confounding variables in test setup and procedures	Medium	Initial food/water intake were not reported but this is not likely to have a significant impact on results.	2	2	4
	22. Outcomes unrelated to exposure	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	1	3
Data presentation and analysis	23. Statistical methods	Not rated	Reviewer implied that the investigators did not conduct a statistical analysis.	NR	NR	NR
	24. Reporting of data	High	Dermal responses were reported for male and female	1	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

			rabbits at different timepoints.			
			Sum of scores:	39	26	53
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	2.038	Overall Score (Rounded):	2.0
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			Medium
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 11. Acute Dermal Irritation Study, [Rupprich and Weigand \(1984a\)](#)

Study Reference:	Rupprich, N., Weigand, W. 1984. Perylimid Testing the acute dermal irritant effects/caustic effects on the rabbit eye. Hoechst Pharma Research Toxicology, Germany. Report No. 84.0228. For Farben Nord, Werk Höchst. HERO ID: 4731534					
Note:	Study was conducted according to OECD TG 404 Acute Dermal Irritation / Corrosion (1981).					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	High	The test substance was identified definitively and the specific form was characterized	1	2	2
	2. Test substance source	Medium	No details were provided about the source and lot number of the test substance.	2	1	2
	3. Test substance purity	Medium	Product contained 80% active ingredient (Perylimid); other components were reported as 10% KOH, 8% diverse organic contaminations, which were not identified, approx 1% inorganic salts, and approx 1% water.	2	1	2
Test setup	4. Negative controls	Not rated	In acute dermal studies, negative controls are not generally used.	NR	NR	NR
	5. Positive controls	Not rated	Positive controls not required for the study.	NR	NR	NR
	6. Randomized allocation	Not rated	Only one group was included, so randomization was not required.	NR	NR	NR
Exposure characterization	7. Preparation and storage of test substance	Low	Amount applied was given but the storage and solubility was not given. 500mg may not dissolve in	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

			0.3ml of 0.9% NaCl solution.			
	8. Consistency of Exposure administration	High ^A		1	1	1
	9. Reporting of doses / concentrations	High	500mg was applied in 0.3ml of 0.9% NaCl solution	1	2	2
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High ^A		1	1	1
	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	Medium	Details were not reported including age and sex.	2	2	4
	14. Adequacy and consistency of animal husbandry conditions	High	Husbandry conditions were reported	1	1	1
	15. Number per group	High ^A		1	1	1
Outcome Assessment	16. Outcome assessment methodology	High ^A		1	2	2
	17. Consistency of outcome assessment	High ^A		1	1	1
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies. Note that the grading of dermal responses is subjective. Training in observing the dermal responses and translating them to a score promotes	NR	NR	NR

REVISED DRAFT – DO NOT CITE OR QUOTE

			harmonization of subjective results.			
	20. Negative Control Response	Not rated	Negative controls were not required for the study.	NR	NR	NR
Confounding/ variable control	21. Confounding variables in test setup and procedures	Medium	Initial food/water intake and respiratory rate were not reported but this is not likely to have a significant impact on results.	2	2	4
	22. Outcomes unrelated to exposure	High ^A		1	1	1
Data presentation and analysis	23. Statistical methods	High	The data was provided, but statistical analysis is not required	1	1	1
	24. Reporting of data	High ^A		1	2	2
			Sum of scores:	25	25	33
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.320	Overall Score (Rounded):	1.3
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	Overall Quality Level:			HIGH
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 12. Eye Irritation Study, [BASF \(1975c\)](#)

Study Reference:	BASF. 1975. Eye Irritation Study. BASF Report XXV/454. Product Safety Basel, BASF Schweiz AG, Switzerland. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731519					
Note:	Study guideline was not indicated in the study report					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASRN number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was not described but it is inferred to be solid state based on the physical/chemical properties of PV29.	2	2	4
	2. Test substance source	Low	No details were provided about the source and lot number of the test substance.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	High	The eye treated with talcum powder served as the negative control	1	2	2
	5. Positive controls	Not rated	Positive control animals are not required for this study.	NR	NR	NR
	6. Randomized allocation	Not rated	Only two individual animals were tested, so randomization is typically not required.	NR	NR	NR
Exposure characterization	7. Preparation and storage of test substance	Low	The study did not discuss details about the preparation and/or storage conditions of the test substance.	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

	8. Consistency of Exposure administration	High ^A		1	1	1
	9. Reporting of doses / concentrations	High ^A		1	2	2
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High	The test typically applies a single dose to one of the eyes of the experimental animal.	1	1	1
	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	Low	Study provided minimal information on the test animal characteristics (<i>e.g.</i> , strain, health status, age).	3	2	6
	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3
	15. Number per group	Medium	Generally at least three animals are used for eye irritation tests. But in this case, study authors used only 2 animals.	2	1	2
Outcome Assessment	16. Outcome assessment methodology	Medium	The method used to score irritation was not discussed. However, it is understood the scoring scale as it is standard for the eye irritation tests. Other details were not discussed (<i>e.g.</i> , criteria for study termination).	2	2	4
	17. Consistency of outcome assessment	Medium	It is inferred that the control (n=1) and treated (n=1) were exposed using the	2	1	2

REVISED DRAFT – DO NOT CITE OR QUOTE

			same method based on details provided in the study. However, the study did not address the measures that the investigators put in place (<i>e.g.</i> , training of staff in scoring) to have consistency in the outcome assessment.			
	18. Sampling adequacy	High	Only two animals were used and in each case one eye was used for test substance and one eye for control substance. The reviewers monitored the animals during and after treatment from 10 min onwards till day 8th.	1	1	1
	19. Blinding of assessors	Not rated	It is not discussed in these studies. Note that the grading of ocular responses is subjective. Training in observing the ocular responses and translating them to a score promotes harmonization of subjective results.	NR	NR	NR
	20. Negative Control Response	High ^A		1	1	1
Confounding/ variable control	21. Confounding variables in test setup and procedures	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	2	6
	22. Outcomes unrelated to exposure	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	1	3
Data presentation and analysis	23. Statistical methods	Not rated	Data not amenable for statistics	NR	NR	NR
	24. Reporting of data	High	Ocular responses were reported for	1	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

			control and treated eyes in both female rabbits.			
			Sum of scores:	38	27	51
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.889	Overall Score (Rounded):	1.9
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			Medium
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 13. Eye Irritation Study, [BASF \(1978a\)](#)

Study Reference:	BASF. 1978. Eye Irritation Study. BASF Report 77/360. Product Safety Basel, BASF Schweiz AG, Switzerland. [as reported in Translated PV29 Tox Summaries, Product Safety Basel, BASF Schweiz AG, Switzerland, January 31, 2018]. HERO ID: 4731520					
Note:	Study guideline was not indicated in the study report					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	Medium	CASRN number was provided (81-33-4) but other expected details were not discussed in the study. For instance, the physical nature of the test substance was not described but it is inferred to be solid state based on the physical/chemical properties of PV29.	2	2	4
	2. Test substance source	Low	No details were provided about the source and lot number of the test substance.	3	1	3
	3. Test substance purity	Low	No details were provided about the test substance purity.	3	1	3
Test setup	4. Negative controls	High	The eye treated with talcum powder served as the negative control	1	2	2
	5. Positive controls	Not rated	Positive control animals are not required for the test type.	NR	NR	NR
	6. Randomized allocation	Not rated	Only two individual animals were tested, so randomization is typically not required.	NR	NR	NR
Exposure characterization	7. Preparation and storage of test substance	Low	The study did not discuss details about the preparation and/or storage conditions of the test substance.	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

	8. Consistency of Exposure administration	High ^A		1	1	1
	9. Reporting of doses / concentrations	High ^A		1	2	2
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High	The test typically applies a single dose to one of the eyes of the experimental animal.	1	1	1
	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	Low	Study provided minimal information on the test animal characteristics (<i>e.g.</i> , strain, health status, age).	3	2	6
	14. Adequacy and consistency of animal husbandry conditions	Low	Study provided minimal information on the adequacy of animal husbandry conditions.	3	1	3
	15. Number per group	High	Three animals were tested, each animal received test substance in one eye and Talcum powder as control in the other eye.	1	1	1
Outcome Assessment	16. Outcome assessment methodology	Medium	The method used to score irritation was not discussed. However, it is understood the scoring scale as it is standard for the eye irritation tests. Other details were not discussed (<i>e.g.</i> , criteria for study termination).	2	2	4
	17. Consistency of outcome assessment	Medium	It is inferred that the control (n=1) and treated (n=1) were exposed using the	2	1	2

REVISED DRAFT – DO NOT CITE OR QUOTE

			same method based on details provided in the study. However, the study did not address the measures that the investigators put in place (<i>e.g.</i> , training of staff in scoring) to have consistency in the outcome assessment.			
	18. Sampling adequacy	High	Three animals were used and in each case one eye was used for test substance and one eye for control substance. The reviewers monitored the animals during and after treatment at different timepoints.	1	1	1
	19. Blinding of assessors	Not Rated	It is not discussed in these studies. Note that the grading of ocular responses is subjective. Training in observing the ocular responses and translating them to a score promotes harmonization of subjective results.	NR	NR	NR
	20. Negative Control Response	High ^A		1	1	1
Confounding/ variable control	21. Confounding variables in test setup and procedures	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	2	6
	22. Outcomes unrelated to exposure	Low	It is not possible to determine if there were confounding variables with the limited information given in the report.	3	1	3
Data presentation and analysis	23. Statistical methods	Not rated	Data not amenable for statistics	NR	NR	NR
	24. Reporting of data	High	Ocular responses were reported for	1	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

			control and treated eyes in male rabbits.			
			Sum of scores:	37	27	50
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.852	Overall Score (Rounded):	1.9
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			Medium
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 14. Eye Irritation Study, [Rupprich and Weigand \(1984b\)](#)

Study Reference:	Rupprich, N, Weigand, W. 1984. Perylimid Testing the acute irritant effects/caustic effects on the rabbit eye. Hoechst Pharma Research Toxicology, Germany. Report No. 84.0229. For Farben Nord, Werk Höchst. HERO ID: 4731524					
Note:	Test was conducted according to the OECD TG 405 Acute Eye Irritation / Corrosion (1981)					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	High	The test substance was identified definitively and the specific form was characterized.	1	2	2
	2. Test substance source	Medium	Source was incompletely reported.	2	1	2
	3. Test substance purity	Medium	Product contained 80% active ingredient (Perylimid); other components were reported as 10% KOH, 8% diverse organic contaminations, which were not identified, approx 1% inorganic salts, and approx 1% water.	2	1	2
Test setup	4. Negative controls	High	The untreated eye served as the negative control.	1	2	2
	5. Positive controls	Not Rated	Positive controls not required for the study.	NR	NR	NR
	6. Randomized allocation	Not Rated	Only one group was included, so randomization is typically not required.	NR	NR	NR
Exposure characterization	7. Preparation and storage of test substance	Low*	Details regarding storage conditions of the test substance in saline were not reported, neither was timeframe between formulation	3	1	3

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Rupprich, N, Weigand, W. 1984. Perylimid Testing the acute irritant effects/caustic effects on the rabbit eye. Hoechst Pharma Research Toxicology, Germany. Report No. 84.0229. For Farben Nord, Werk Höchst. HERO ID: 4731524					
			preparation and use. Amount applied was given but the storage and solubility was not given. 100mg may not dissolve in 0.05ml of 0.9% NaCl solution.			
	8. Consistency of Exposure administration	High ^A		1	1	1
	9. Reporting of doses / concentrations	High	100mg was applied in 0.3ml of 0.9% NaCl solution	1	2	2
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High ^A		1	1	1
	12. Exposure route and method	High ^A		1	1	1
Test organisms	13. Test animal characteristics	Medium	Details were not reported including age and sex.	2	2	4
	14. Adequacy and consistency of animal husbandry conditions	High	Husbandry conditions were reported	1	1	1
	15. Number per group	High ^A		1	1	1
Outcome Assessment	16. Outcome assessment methodology	High ^A		1	2	2
	17. Consistency of outcome assessment	High ^A		1	1	1
	18. Sampling adequacy	High ^A		1	1	1

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Rupprich, N, Weigand, W. 1984. Perylimid Testing the acute irritant effects/caustic effects on the rabbit eye. Hoechst Pharma Research Toxicology, Germany. Report No. 84.0229. For Farben Nord, Werk Höchst. HERO ID: 4731524					
	19. Blinding of assessors	Not Rated	No subjective outcomes were assessed.	NR	NR	NR
	20. Negative Control Response	High ^A		1	1	1
Confounding/ variable control	21. Confounding variables in test setup and procedures	High ^A		1	2	2
	22. Outcomes unrelated to exposure	High ^A		1	1	1
Data presentation and analysis	23. Statistical methods	High	The data was provided, but statistical analysis is not required	1	1	1
	24. Reporting of data	High ^A		1	2	2
			Sum of scores:	26	28	34
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.214	Overall Score (Rounded):	1.2
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	Overall Quality Level:			HIGH

Footnote A: This metric met the criteria for high confidence as expected for this type of study.

Table 15. Local Lymph Node Assay, [Johnson \(1999\)](#)

Study Reference:	Johnson, I.R. 1999. Perylimid F: Local Lymph Node Assay. Central Toxicology Laboratory, UK. Project No. CTL/P/6194. For BASF Aktiengesellschaft, Germany. HERO ID: 4731537.					
Note:	Study report indicates that test was conducted according to OECD TG 406: Skin sensitization (1992)					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	High	The test substance was identified definitively and the specific form was characterized	1	2	2
	2. Test substance source	High	Test item was received by the submitter and the batch number was provided.	1	1	1
	3. Test substance purity	High	Given as 90% and the dose calculations were adjusted to purity	1	1	1
Test setup	4. Negative and vehicle controls	High ^A		1	2	2
	5. Positive controls	High	Positive control study was conducted within 6 months of study and was appropriate.	1	1	1
	6. Randomized allocation	Low	Allocation of animals into study groups was not reported.	3	1	3
Exposure characterization	7. Preparation and storage of test substance	Medium	Details regarding storage conditions of the test	2	1	2

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Johnson, I.R. 1999. Perylimid F: Local Lymph Node Assay. Central Toxicology Laboratory, UK. Project No. CTL/P/6194. For BASF Aktiengesellschaft, Germany. HERO ID: 4731537.					
			substance in propylene glycol were not reported.			
	8. Consistency of exposure administration	High ^A		1	1	1
	9. Reporting of doses / concentrations	High	The administered doses were reported without ambiguity.	1	2	2
	10. Exposure frequency and duration	High ^A		1	1	1
	11. Number of exposure groups and dose spacing	High	It is unclear if the highest concentration was high enough to induce a response.	1	1	1
	12. Exposure route and method	High	The route and method of exposure were reported.	1	1	1
Test organisms	13. Test animal characteristics	Medium	Details were not reported including age, health status, and starting body weight.	2	2	4
	14. Adequacy and consistency of animal husbandry conditions	High ^A	All husbandry conditions were reported and the only difference was the exposure.	1	1	1
	15. Number per group	High ^A		1	1	1
Outcome Assessment	16. Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcomes of interest and	1	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Johnson, I.R. 1999. Perylimid F: Local Lymph Node Assay. Central Toxicology Laboratory, UK. Project No. CTL/P/6194. For BASF Aktiengesellschaft, Germany. HERO ID: 4731537.					
			was sensitive for the outcome of interest.			
	17. Consistency of outcome assessment	High	Details of the outcome of assessment protocols and reported outcomes were assessed consistently.	1	1	1
	18. Sampling adequacy	High ^A		1	1	1
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies.	NR	NR	NR
	20. Negative control response	High	The biological responses of the negative control group were adequate.	1	1	1
Confounding/ variable control	21. Confounding variables in test setup and procedures	High ^A		1	2	2
	22. Outcomes unrelated to exposure	High	Due to heavy precipitation of the test substance the bacterial lawn could only be evaluated to the penultimate highest dose.	1	1	1
Data presentation and analysis	23. Statistical methods	High	The data was reported, but the statistically analysis was not required as the test substance did not cause significant change.	1	1	1

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Johnson, I.R. 1999. Perylimid F: Local Lymph Node Assay. Central Toxicology Laboratory, UK. Project No. CTL/P/6194. For BASF Aktiengesellschaft, Germany. HERO ID: 4731537.					
	24. Reporting of data	High	Data was presented for all outcomes.	1	2	2
			Sum of scores:	27	30	35
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.167	Overall Score (Rounded):	1.2
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	Overall Quality Level:			HIGH
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 16. Study of the Mutagenic Potential in Strains of Salmonella typhimurium (AMES Test) and Escherichia coli, [Jung and Weigand \(1983\)](#)

Study Reference:	Jung, R., Weigand, W. 1983. Perylimid Study of the Mutagenic Potential in Strains of <i>Salmonella typhimurium</i> (AMES Test) and <i>Escherichia coli</i> . Hoechst Aktiengesellschaft, Germany. Report No. 83.0695. For Hoechst, Fahrenforschung, Germany. HERO ID: 4731535.					
Note:	Study report did not indicate the authors followed a test guideline					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	High	The test substance was identified definitively and the specific form was characterized	1	2	2
	2. Test substance source	Medium	The source was incompletely reported.	2	1	2
	3. Test substance purity	High	See note at the bottom of the table.	1	1	1
Test setup	4. Negative controls	High	Solvent control was used as negative control	1	2	2
	5. Positive controls	High	The positive controls were included and the response was appropriate.	1	2	2
	6. Assay procedure	High ^A		1	1	1
	7. Standards for test	Not rated	This metric is not applicable for this endpoint	NR	NR	NR
Exposure characterization	8. Preparation and storage of test substance	Medium	The test substance was prepared on the day of the test, but storage information	2	1	2

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Jung, R., Weigand, W. 1983. Perylimid Study of the Mutagenic Potential in Strains of <i>Salmonella typhimurium</i> (AMES Test) and <i>Escherichia coli</i> . Hoechst Aktiengesellschaft, Germany. Report No. 83.0695. For Hoechst, Fahrenforschung, Germany. HERO ID: 4731535.					
			was not provided.			
	9. Consistency of exposure administration	High ^A		1	1	1
	10. Reporting of concentrations	High	The tested doses were reported without ambiguity.	1	2	2
	11. Exposure duration	High	48 to 72hr with and without metabolic activation.	1	2	2
	12. Number of exposure groups and dose spacing	High ^A		1	1	1
	13. Metabolic activation	High	Metabolic activation is reported and performed using Mammalian Microsomal Fraction S9 Mix	1	1	1
Test Model	14. Test model	High	Bacterial and <i>Salmonella typhimurium</i> was chosen based on historical success in in vitro experiments.	1	2	2
	15. Number per group	High	The number of exposed cells/ replicate was not reported. The number of replicates/ concentration was appropriate.	1	1	1

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Jung, R., Weigand, W. 1983. Perylimid Study of the Mutagenic Potential in Strains of <i>Salmonella typhimurium</i> (AMES Test) and <i>Escherichia coli</i> . Hoechst Aktiengesellschaft, Germany. Report No. 83.0695. For Hoechst, Fahrenforschung, Germany. HERO ID: 4731535.					
Outcome Assessment	16. Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive	1	2	2
	17. Consistency of outcome assessment	High	Details of the outcome of assessment protocols and reported outcomes were assessed consistently	1	1	1
	18. Sampling adequacy	High ^A		1	2	2
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies.	NR	NR	NR
Confounding/variable control	20. Confounding variables in test setup and procedures	High ^A		1	2	2
	21. Confounding variables in outcomes unrelated to exposure	High ^A		1	1	1
Data presentation and analysis	22. Data analysis	High	Statistical methods, calculation and methods were not required	1	1	1
	23. Data interpretation	High	Evaluation criteria appeared to be limited to positive controls, defined as a significant increase in	1	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Jung, R., Weigand, W. 1983. Perylimid Study of the Mutagenic Potential in Strains of <i>Salmonella typhimurium</i> (AMES Test) and <i>Escherichia coli</i>. Hoechst Aktiengesellschaft, Germany. Report No. 83.0695. For Hoechst, Fahrenforschung, Germany. HERO ID: 4731535.					
			revertant colonies			
	24. Cytotoxicity data	Not rated	This was not a cytotoxicity test rather a mutagenicity test. this Metric should not be applied	NR	NR	NR
	25. Reporting of data	High ^A		1	2	2
			Sum of scores:	23	33	35
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.061	Overall Score (Rounded):	1.1
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	Overall Quality Level:			HIGH
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 17. Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro, [Wollny \(2012\)](#)

Study Reference:	Wollny, H. 2012. Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro (V79/HPRT) with Paliogen Violet 5011. Harlan Cytotest Cell Research GmbH, Germany. Report No. 1443105. For BASF SE, Germany. HERO ID: 4731536.					
Note:	Study report indicates it was conducted according to OECD TG 467/ OPPTS 870.5300					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	High	The test substance was identified definitively, and the specific form was characterized	1	2	2
	2. Test substance source	Medium	The source was incompletely reported.	2	1	2
	3. Test substance purity	High	Given as 90% and the dose calculations were adjusted to purity	1	1	1
Test setup	4. Negative controls	High	Solvent control was used as negative control	1	2	2
	5. Positive controls	High	The positive controls were included and the response was appropriate (induction of positive effect).	1	2	2
	6. Assay procedure	High ^A		1	1	1
	7. Standards for test	High	Mutant colonies per 10 ⁶ cell identified in solvent control should be within the laboratory historical controls and positive control substance is expected to produce significant increase in	1	1	1

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Wollny, H. 2012. Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro (V79/HPRT) with Paliogen Violet 5011. Harlan Cytotest Cell Research GmbH, Germany. Report No. 1443105. For BASF SE, Germany. HERO ID: 4731536.					
			mutant colony frequency.			
Exposure characterization	8. Preparation and storage of test substance	Medium	The test substance was prepared on the day of the test, but storage information was not provided.	2	1	2
	9. Consistency of exposure administration	High ^A		1	1	1
	10. Reporting of concentrations	High	The tested doses were reported without ambiguity.	1	2	2
	11. Exposure duration	High	4hr and 24hr with and without metabolic activation	1	2	2
	12. Number of exposure groups and dose spacing	High ^A		1	1	1
	13. Metabolic activation	High	Metabolic activation is reported and performed using Mammalian Microsomal Fraction S9 Mix	1	1	1
Test Model	14. Test model	High	V79 cell line was chosen based on historical success in in vitro experiments.	1	2	2
	15. Number per group	High	The number of exposed cells/replicates was not reported. The number of replicates/ concentration was appropriate	1	1	1
Outcome Assessment	16. Outcome assessment methodology	High	The outcome assessment methodology	1	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Wollny, H. 2012. Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro (V79/HPRT) with Paliogen Violet 5011. Harlan Cytotest Cell Research GmbH, Germany. Report No. 1443105. For BASF SE, Germany. HERO ID: 4731536.					
			addressed the intended outcome of interest and was sensitive			
	17. Consistency of outcome assessment	High	Details of the outcome of assessment protocols and reported outcomes were assessed consistently	1	1	1
	18. Sampling adequacy	High ^A		1	2	2
	19. Blinding of assessors	Not rated	It is not typically discussed in these studies.	NR	NR	NR
Confounding/ variable control	20. Confounding variables in test setup and procedures	High	There were no differences reported among study groups apart from precipitation of the test substance in the higher doses.	1	2	2
	21. Confounding variables in outcomes unrelated to exposure	High ^A		1	1	1
Data presentation and analysis	22. Data analysis	High	Statistical methods, calculation and methods were presented	1	1	1
	23. Data interpretation	High	Evaluation criteria appeared to be limited to positive controls, defined as a significant increase in revertant colonies	1	2	2
	24. Cytotoxicity data	Not rated	This is not a cytotoxicity test rather a	NR	NR	NR

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Wollny, H. 2012. Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro (V79/HPRT) with Paliogen Violet 5011. Harlan Cytotest Cell Research GmbH, Germany. Report No. 1443105. For BASF SE, Germany. HERO ID: 4731536.					
			mutagenicity test, \ so this metric is not applicable			
	25. Reporting of data	High ^A		1	2	2
			Sum of scores:	24	34	36
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:	1.059	Overall Score (Rounded):	1.1
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	Overall Quality Level:			HIGH
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

Table 18. Effects of Subchronically Inhaled Carbon Black, [Elder et al. \(2005\)](#)

Study Reference:	Elder et al., 2005. Effects of Subchronically Inhaled Carbon Black in Three Species. I. Retention Kinetics, Lung Inflammation, and Histopathology. HERO ID: 88194					
Note:	This study analyzed the inhalation effects of Carbon Black, an analogue of C.I. Pigment Violet 29.					
Domain	Metric	Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]	Comments	Metric Score	Metric Weighting Factor	Weighted Score
Test Substance	1. Test substance identity	High	The test substance was identified definitively, and the specific form was characterized	1	2	2
	2. Test substance source	High	The Test Substance source was reported	1	1	1
	3. Test substance purity	High	Test substance purity was reported	1	1	1
Test setup	4. Negative controls	High	Negative controls were reported	1	2	2
	5. Positive controls	Not rated	Positive control animals are not required for this study.	NR	NR	NR
	6. Randomized allocation	High	Test organisms were randomly allocated to exposure groups	1	1	1
Exposure characterization	7. Preparation and storage of test substance	High	Test substance preparation was fully reported.	1	1	1
	8. Consistency of Exposure administration	High	Details of exposure administration was fully reported.	1	1	1
	9. Reporting of doses / concentrations	High		1	2	2

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Elder et al., 2005. Effects of Subchronically Inhaled Carbon Black in Three Species. I. Retention Kinetics, Lung Inflammation, and Histopathology. HERO ID: 88194					
	10. Exposure frequency and duration	High		1	1	1
	11. Number of exposure groups and dose spacing	High		1	1	1
	12. Exposure route and method	High		1	1	1
Test organisms	13. Test animal characteristics	High		1	2	2
	14. Adequacy and consistency of animal husbandry conditions	Not Assessed		NA	NA	NA
	15. Number per group	High	Reported	1	1	1
Outcome Assessment	16. Outcome assessment methodology	High		1	2	2
	17. Consistency of outcome assessment	High		1	1	1
	18. Sampling adequacy	High		1	1	1
	19. Blinding of assessors	High		1	1	1
	20. Negative Control Response	High	No effects reported in controls	1	1	1
Confounding/variable control	21. Confounding variables in test setup and procedures	High	No confounding variables	1	2	2
	22. Outcomes unrelated to exposure	Med	Not Reported	2	1	2
Data presentation and analysis	23. Statistical methods	High		1	1	1
	24. Reporting of data	High		1	2	2
			Sum of scores:			
High	Medium	Low	Overall Score = Sum of Weighted Scores/Sum of	23	Overall Score (Rounded):	29

REVISED DRAFT – DO NOT CITE OR QUOTE

Study Reference:	Elder et al., 2005. Effects of Subchronically Inhaled Carbon Black in Three Species. I. Retention Kinetics, Lung Inflammation, and Histopathology. HERO ID: 88194					
			Metric Weighting Factors:			
≥ 1 and < 1.7	≥ 1.7 and < 2.3	≥ 2.3 and ≤ 3	1.034	1	Overall Quality Level:	High
Footnote A: This metric met the criteria for high confidence as expected for this type of study.						

References

- [BASF](#). (1975a). Acute inhalation toxicity with rats. BASF report XXV/454. In Product Safety Basel. (XXV/454). Switzerland: BASF Schweiz AG.
- [BASF](#). (1975b). Acute oral toxicity with rats. BASF report XXV/454. (XXV/454). Switzerland: BASF Schweiz AG.
- [BASF](#). (1975c). Eye irritation study. BASF report XXV/454. In Product Safety Basel. (XXV/454). Switzerland: BASF Schweiz AG.
- [BASF](#). (1975d). Skin irritation study. BASF report XXV/454. In Product Safety Basel. (XXV/454). Switzerland: BASF Schweiz AG.
- [BASF](#). (1975e). Summary of toxicological investigations with CAS 81-33-4, Acute intraperitoneal toxicity with mice. BASF Report XXV/454. In Product Safety Basel. (XXV/454). Switzerland: BASF Schweiz AG.
- [BASF](#). (1978a). Eye irritation study. BASF report 77/360. In Product Safety Basel. (77/360). Switzerland: BASF Schweiz AG.
- [BASF](#). (1978b). Study report for CAS 81-33-4, Acute inhalation toxicity with rats. BASF report 77/360. In Product Safety Basel. (77/360). Switzerland: BASF Schweiz AG.
- [BASF](#). (1978c). Study report for CAS 81-33-4, Acute intraperitoneal toxicity with mice. BASF report 77/360. In Product Safety Basel. Switzerland: BASF Schweiz AG.
- [BASF](#). (1978d). Study report for CAS 81-33-4, acute oral toxicity with rats. BASF report 77/360. In Product Safety Basel. (77/360). Switzerland: BASF Schweiz AG.
- [BASF](#). (1978e). Study report for CAS 81-33-4, skin irritation study. BASF report 77/360. In Product Safety Basel. (77/360). Switzerland: BASF Schweiz AG.
- [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>.
- [Johnson, IR](#). (1999). Perylimid F: Local lymph node assay. Project no. CTL/P/6194. (CTL/P/6194). Germany: BASF Aktiengesellschaft.
- [Jung, R; Weigand, W](#). (1983). Perylimid study of the mutagenic potential in strains of salmonella typhimurium (Ames Test) and escherichia coli. (83.0695). Germany: Hoechst Aktiengesellschaft.
- [Rupprich, N; Weigand, W](#). (1984a). Perylimid testing the acute dermal irritant effects/caustic effects on the rabbit eye. (84.0228). Germany: Hoechst AG, Pharma Research Toxicology and Pathology.
- [Rupprich, N; Weigand, W](#). (1984b). Perylimid testing the acute irritant effects/caustic effects on the rabbit eye. (84.0229). Germany: Hoechst AG, Pharma Research Toxicology and Pathology.
- [Rupprich, N; Weigand, W](#). (1984c). Testing the acute oral toxicity in the male and female Wistar rat. (84.0225). Germany: Hoechst AG, Pharma Research Toxicology and Pathology.
- [Stark, D; Treumann, S; van Ravenzwaay, B](#). (2013). Reproduction/developmental toxicity screening test in Wistar rats oral administration (gavage). (80R0223/11C162). Germany: BASF SE.
- [U.S. EPA](#). (2018). 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_tsc_a_05-31-18.pdf.
- [Wollny, H](#). (2012). Gene mutation assay in Chinese hamster V79 cells in vitro (V79/HPRT) with paliogen violet 5011. (1443105). Germany: BASF SE.