C.I. Pigment Violet 29 (81-33-4) Systematic Review: Supplemental File for the TSCA Risk Evaluation

Data Evaluation Scoring Sheets

Updated Document
April, 2019

The updated *C.I. Pigment Violet 29 (81-33-4) Systematic Review: Supplemental File for the TSCA Risk Evaluation* contains the data evaluation scoring sheets for the 24 full study reports that the Agency used to inform the human health hazard, environmental hazard, environmental fate and physical-chemical properties of C.I. Pigment Violet 29 (PV29). These full study reports were used to develop the Draft Risk Evaluation for PV29. The EPA initially released the SR Supplemental File without the EPA's reviewer comments on the metric score determinations due to concerns that the comments might have CBI information. As part of the CBI substantiation process, the EPA reviewed the CBI claims in accordance with the processes set forth in the Agency regulations and has made the full study reports publicly available. Details about this process are provided in the March 21, 2019 memo, *Transmission of Background Materials Previously Claimed as Confidential Business Information (CBI) for the Toxic Substances Control Act's Scientific Advisory Committee on Chemicals (TSCA SACC) Reviewing the Draft Risk Evaluation for C.I. Pigment Violet 29 (PV29)* (Agency Docket ID: EPA-HQ-OPPT-2018-0604-0022). As a result, the reviewers comments will be made publicly available in this updated document. In addition, the EPA re-reviewed the studies and determined that two acute inhalation studies (Pg 20-25) were found to be *Unacceptable* for use in the risk assessment. The EPA also determined that two acute oral toxicity studies (Pg 14-17) and two eye irritation studies (pg 38-41) were downgraded to *Medium* confidence, while two acute intraperitoneal (Pg 26-29) were downgraded to *Low* confidence. These changes are reflected in this document, where all revised metric scores are denoted by an *.

Study Reference:	BASF. 2013. Physical-Chemical properties of "Paliogen Violet 5011". BASF Study No. 11L00105. Competence Center Analytics, BASF SE, D-67056 Ludwigshafen. Test Completion Date: November, 28, 2011. HERO ID: 4731544		
Note:	BASF (2013) reported various physical-chemical properties and only the confidence of the melting point is evaluated.		
Domain/Metric	**Description/ Definition**	**Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]**	**Comment**
Representativeness	The information or data reflects the data and chemical substance type.	High	The data was measured for the substance of interest.
Appropriateness	The information or data reflects anticipated results based on chemical structural features or behaviors.	High	The measured value is consistent with the nature of the substance
Evaluation/ Review	The information or data reported has reliable review.	Medium	The data is from a source that is not described as poor-reviewed by experts in the field or are broadly available to the public for review and use, but is known. EPA plans to refine the criteria to clearly indicate the circumstances would make the data source to be of medium/low confidence for this domain/metric.
Reliability/ Unbiased (Method Objectivity)	The method for producing the data/information is not biased towards a particular product or outcome.	High	The methodology is designed to determine the endpoint of interest.
Reliability/ Analytic Method	The information or data reported is from a reliable method.	High	The study used a standard and generally accepted method for this type of study.
		Overall Quality Level	**HIGH**

Study Reference:	BASF. 2013. Physical-Chemical properties of "Paliogen Violet 5011". BASF Study No. 11L00105. Competence Center Analytics, BASF SE, D-67056 Ludwigshafen. Test Completion Date: November, 28, 2011. HERO ID: 4731544		
Note:	BASF (2013) reported various physical-chemical properties and only the confidence of the Log Kow (octanol/water partition coefficient) is evaluated.		
Domain/Metric	**Description/ Definition**	**Qualitative Determination [i.e., High, Medium, Low, Unacceptable, or Not rated]**	**Comment**
Representativeness	The information or data reflects the data and chemical substance type.	High	The data was measured for the substance of interest.
Appropriateness	The information or data reflects anticipated results based on chemical structural features or behaviors.	**Unacceptable***	The substance is not soluble in either octanol or water. Therefore, partitioning between the media cannot be determined. EPA plans to refine the criteria to clearly indicate that these circumstances fall under an unacceptable confidence. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not Rated* to *Unacceptable* .
Evaluation/ Review	The information or data reported has reliable review.	Medium*	The data is from a source that is not described as poor-reviewed by experts in the field or are broadly available to the public for review and use, but is known. EPA plans to refine the criteria to clearly indicate the circumstances would make the data source to be of medium confidence for this domain/metric. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not Rated* to *Medium.*
Reliability/ Unbiased (Method Objectivity)	The method for producing the data/information is not biased towards a particular product or outcome.	Not Rated	Data source does not provide information to determine the method objectivity (unbiased method). Thus the domain/metric was not rated.
Reliability/ Analytic Method	The information or data reported is from a reliable method.	**Unacceptable**	The substance is not soluble in either octanol or water. Therefore, partitioning between the media cannot be determined. This analytical method is not appropriate.
	Overall Quality Level		**UNACCEPTABLE[1]**
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, two of the metrics were rated as unacceptable. As such, the study is considered unacceptable.			

Study Reference:	BASF. 1999. Determination of the Biodegradability of Perylimid F in the Manometric Respirometry Test according to GLP, EN 45001 and ISO 9002. Study conducted by BASF Aktiengesellschaft Ecology and Environmental Analytics Laboratory of Ecology D-67056 Ludwigshafen (Study Completion Date: July, 1999). HERO ID: 4731543					
Note	Conducted according to OECD Guideline 301F					
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	CAS, chemical name, production number, state and date of production were all reported	1	2	2
	2. Test Substance Purity	High	Purity reported as 98.9%.	1	1	1
Test Design	3. Study Controls	High	Blank control and reference substance were included (Aniline); deviation and control chemical were acceptable according to test validity criteria of the guideline.	1	2	2
	4. Test Substance Stability	High	Homogeneity, storage conditions, instability controls were all reported.	1	1	1
Test Conditions	5. Test Method Suitability	Medium*	Media concentrations were provided in terms of nominal concentrations (100 mg/L) which was far higher than the limit of solubility. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* to reflect the test concentration being above the limit of solubility of the test material.	2	1	2
	6. Testing Conditions	High	Biodegradation values were measured and reported (28 days) according to reporting recommendations of Guideline. Test temperatures throughout the test were not explicitly reported, but the study authors indicated that the test was conduicted "at room temperature".	1	2	2
	7. Testing Consistency	High	Five control samples and seven test samples were conducted under the same condition.	1	1	1
	8. System Type and Design	Not Rated	Not an equilibrium test.	NR	NR	NR
Test Organisms	9. Test Organism - Degradation	High	Inoculum source reported as municipal activated sludge from laboratory wastewater treatment plants fed with municipal sewage which is appropriate.	1	2	2
	10. Test Organism - Partitioning	Not Rated	This is not a partitioning test.	NR	NR	NR
Outcome Assessment	11. Outcome Assessment Methodology	High	The test methodology addressed the intended outcome of interest (biodegradation according to the parameters measured).	1	1	1
	12. Sampling Methods	Medium*	Sampling methods were not specifically discussed, but the results of daily analysis of the test variables were reported. The asterisk (*) indicates that the confidence was reevaluated and changed from *high* to *medium* to more accurately reflect the lack of specific discussion of sampling methods.	2	1	2
Confounding/ Variable Control	13. Confounding Variables	Medium	The result (Measured BOD) of one blank sample deviated from other 6 test samples. The authors acknowledged and disregarded this sample.	2	1	2

Confounding/ Variable Control	14. Outcomes Unrelated to Exposure	Medium	6 out of 7 test samples showed similar results, the degradation rate of all test samples did not show any inhibition from the test substance; One blank sample showed anomalous results discussed by the authors. The viability of organism was well maintained.	2	1	2
Data Presentation and Analysis	15. Data Reporting	High[A]		1	2	2
	16. Statistical Methods & Kinetic Calculations	Medium	No statistical analyses were conducted; however, sufficient data were provided to conduct an independent statistical analysis.	2	1	2
Other	17. Verification or Plausibility of Results	High	Reported values were within expected range as defined by reference substance(s); Aniline.	1	1	1
	18. QSAR Models	Not Rated	QSAR models were not used as part of this study.	NR	NR	NR
			Sum of scores:	**20**	**20**	**25**
High	Medium	Low	**Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:**	**1.250**	**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.						

Study Reference:	BASF. 1999. Determination of the Inhibition of Oxygen Consumption by Activated Sludge by Perylimid F in the Activated Sludge Respiration Inhibition Test according to GLP, EN 45001 and ICO 9002. Study conducted by BASF Aktiengesellschaft Ecology and Environmental Analytics Laboratory of Ecology D-67056 Ludwigshafen (Study Completion Date: March, 1999). HERO ID: 4731542					
Note	Conducted according to OECD Guideline 209					
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	CAS, chemical name, production number and date, as well as the specific form of the test substance are all reported.	1	2	2
	2. Test Substance Purity	High	Purity 98.9% reported by analysis	1	1	1
Test Design	3. Study Controls	High	Blank Control was included and deviation of blank control was reported as <15%. A reference substance was also included.	1	2	2
	4. Test Substance Stability	High	Homogeneity, storage conditions, instability control were all reported and appeared to be appropriate for the test substance.	1	1	1
Test Conditions	5. Test Method Suitability	Medium*	Media concentrations were provided in terms of nominal concentrations (1000 mg/L) and were not measured. The reported limit of solubility (2800 mg/L) was not consistent with the limit of solubility of this chemical. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* to reflect the solubility reported in the study.	2	1	2
	6. Testing Conditions	High	Testing conditions were recorded and were suitable for the test substance	1	2	2
	7. Testing Consistency	High	Three blank controls, the test substance were conducted under the same conditions.	1	1	1
	8. System Type and Design	Not Rated	This metric is not applicable as this is not an equilibrium test	NR	NR	NR
Test Organisms	9. Test Organism - Degradation	High	Inoculum source was a laboratory wastewater plant treating municipal and synthetic sewage; the dry substance concentration of the inoculum was reported as 1 g/L	1	2	2
	10. Test Organism - Partitioning	Not Rated	This metric is not applicable as this is not a partitioning study	NR	NR	NR
Outcome Assessment	11. Outcome Assessment Methodology	High	The outcome assessment methodology is acceptable to determine the inhibition of oxygen consumption by activated sludge.	1	1	1
	12. Sampling Methods	Medium	Sampling methods were not specifically discussed, but the results of daily analysis of the test variables were reported so this is not expected to impact the results of the test.	2	1	2

Confounding/ Variable Control	13. Confounding Variables	High	One study group was used as this was conducted as a limit test. No confounding variables were observed or reported by the study authors.	1	1	1
	14. Outcomes Unrelated to Exposure	High	Deviation of blank controls were reported to be <15%, which demonstrated the health of the test organism.	1	1	1
Data Presentation and Analysis	15. Data Reporting	High	Study was conducted as a limit test, so no effects were observed in the study group. Study authors calculated and reported EC20, EC50, and EC80 of reference substance as well as the control.	1	2	2
	16. Statistical Methods & Kinetic Calculations	Not Rated	Statistical analysis was not conducted as no adverse effects were reported.	NR	NR	NR
Other	17. Verification or Plausibility of Results	High	Reported values were within expected range as defined by the reference substance, 3,5-dichlorophenol.	1	1	1
	18. QSAR Models	Not Rated	QSAR models were not used as part of this study. *Note that this metric has been updated, as it was originally evaluated for a metric that is not part of the data quality criteria for fate data.	NR	NR	NR
			Sum of scores:	16	19	21
High	Medium	Low	**Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:**	1.105	**Overall Score (Rounded):**	1.1
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3	**Overall Quality Level:**			**HIGH**

Study Reference:	BASF (2012). H-28548: Paliogen Violet 5011, *Lemna gibba* L. CPCC 310 Growth Inhibition Test according to OECD Guideline No. 221. Study conducted by Institute of Industrial Organic Chemistry, Branch Pszczyna Department of Ecotoxicology. (Study Completion Date: October, 2012), Pszczyna, Poland. HERO ID: 4731540					
Note:	Conducted according to OECD TG 221 (2006)					
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	Test substance was reported as Paliogen Violet 5011, which shares the same chemical name with PV29.	1	2	2
	2. Test substance source	High	Test material was provided by the study sponsor and reported.	1	1	1
	3.Test substance purity	Medium	Although the test substance purity was not reported in the study, the test concentrations were adequately quantified throughout the test.	2	1	2
Test setup	4. Negative controls	High[A]		1	2	2
	5. Negative control response	High	No effects were seen in the negative controls.	1	1	1
	6. Randomized allocation	HIgh	Study report mentioned that replicates were arranged at random and rearranged repeatedly.	1	1	1
Exposure characterization	7. Experimental System/Test Media Preparation	High[A]		1	2	2
	8. Consistency of Exposure administration	High[A]		1	1	1
	9. Exposure Duration and Frequency	High[A]		1	2	2
	10. Measurement of Test Substance Concentration	High	Measured concentrations of all test concentrations reported.	1	1	1
	11. Number of exposure groups and dose spacing	High[A]		1	1	1
	12. Testing at or Below Solubility Limit	High	Study authors conducted the experiments above the solubility limit with no solvent and quantified the test concentrations.	1	1	1
Test organisms	13. Test organism characteristics	High	Test organism was *Lemna gibba* obtained from a laboratory.	1	2	2
	14. Acclimatization and Pretreatment Conditions	Medium*	Although details about the acclimization and pretreatment conditions were not reported, this is unlikely to affect the study results. The asterisk (*) indicates that the confidence was reevaluated and changed from Not Rated to Medium.	2	1	2
	15. Number of Organisms and Replicates per group	High[A]		1	1	1
	16. Adequacy of Test Conditions	High[A]		1	1	1
Outcome assessment	17. Outcome assessment methodology	High[A]		1	2	2

Outcome assessment	18. Consistency of outcome assessment	High[A]		1	1	1
Confounding/ variable control	19. Confounding variables in test setup and procedures	High[A]		1	2	2
	20. Outcomes unrelated to exposure	Not Rated	No unexpected outcomes were reported.	NR	NR	NR
Data presentation and analysis	21. Statistical methods	High	Probit analysis was used to calculate slope of the dose response.	1	1	1
	22. Reporting of data	High[A]		1	2	2
	23. Explanation of Unexpected Outcomes	Not Rated	No unexplained outcomes were reported.	NR	NR	NR
			Sum of scores:	23	29	31
High	Medium	Low	**Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:**	1.069	**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.						

Study Reference:	BASF (2012). H-28548: Paliogen Violet 5011, *Daphnia magna,* Acute immibolization test. Study conducted by Institute of Industrial Organic Chemistry, Branch Pszczyna Department of Ecotoxicology. (Study Completion Date: May, 2012), Pszczyna, Poland. HERO ID: 4731541					
Note	Conducted according to the OECD 202 Test Guideline (2004)					
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	Pages 37 and 46 indicated Paliogen Violet, the reported test substance, is comprised of PV 29 as indicated by the CASRN.	1	2	2
	2. Test substance source	High	Pages 37 and 46 indicated test material was sourced from the manufacturer.	1	1	1
	3.Test substance purity	Medium	Study report indicated that the Test material is PV 29, but does not specify the chemical purity. The test concentration of the definitive test was analytically verified by mass spectroscpy	2	1	2
Test setup	4. Negative controls	High	Negative controls and reference test were used.	1	2	2
	5. Negative control response	High	No immibilization/mortality was observed.	1	1	1
	6. Randomized allocation	Low	There was only one test concentration, but it was not mentioned whether indivituals were randomly allocated.	3	1	3
Exposure characterization	7. Experimental System/Test Media Preparation	High[A]		1	2	2
	8. Consistency of Exposure administration	High	Conducted as a limit test, concentrations were measured at start and termination of the test to quantify degredation.	1	1	1
	9. Exposure Duration and Frequency	High[A]		1	2	2
	10. Measurement of Test Substance Concentration	High[A]		1	1	1
	11. Number of exposure groups and dose spacing	High	Test was conducted as a limit test based on results of range-finding test.	1	1	1
	12. Testing at or Below Solubility Limit	High	Test was conducted as a limit test based on results of range-finding test. As a result, test was conducted as a limit test and test concentrations were analytically confirmed to match the reported limit of solubility for the test material.	1	1	1
Test organisms	13. Test organism characteristics	High[A]		1	2	2
	14. Acclimatization and Pretreatment Conditions	High[A]		1	1	1
	15. Number of Organisms and Replicates per group	High[A]		1	1	1
	16. Adequacy of Housing Conditions	High[A]		1	1	1
Outcome assessment	17. Outcome assessment methodology	High[A]		1	2	2

Outcome assessment	18. Consistency of outcome assessment	High[A]		1	1	1
Confounding/ variable control	19. Confounding variables in test setup and procedures	High	There were no reported confounding variables in the experiments that could influence the outcome assessment.	1	2	2
	20. Outcomes unrelated to exposure	High	There were no reported differences among the test groups that could influence the outcome assessment.	1	1	1
Data presentation and analysis	21. Statistical methods	Not Rated	No statistics necessary because the test was conducted as a limit test.	NR	NR	NR
	22. Reporting of data	High		1	2	2
	23. Explanation of Unexpected Outcomes	Not Rated	No unexplained outcomes and no effects were observed up to the highest test concentration.	NR	NR	NR
			Sum of scores:	24	29	32
High	Medium	Low	**Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:**	1.103	**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.						

Study Reference:	BASF. 1988. Testing the acute toxicity in the fish model Zebra danio (B*rachydanio rerio*) over the course of 96 hours. Study conducted by Pharma Research Toxicology and Pathology, Hoechst Corporation (Study Completion Date: July 1st, 1988), Frankfurt, Germany. HERO ID: 4731539					
Note	Conducted according to the OECD 203 Test Guideline (1984)					
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	Test substance was reported as perylimid, which is an European name for PV 29.	1	2	2
	2. Test substance source	Medium	Test substance source was not indicated. See note at the bottom of the table.	2	1	2
	3.Test substance purity	High*	Purity was reported as > 95%. The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *High* , because uncertainties regarding the reported solubility limit of the chemical are better suited to metrics 10 and 12.	1	1	1
Test setup	4. Negative controls	High[A]		1	2	2
	5. Negative control response	High	No mortality was reported in the controls.	1	1	1
	6. Randomized allocation	High[A]	Section 4.7 indicated that individuals were randomly allocated among the test vessels.	1	1	1
Exposure characterization	7. Experimental System/ Test Media Preparation	High[A]		1	2	2
	8. Consistency of Exposure administration	High[A]		1	1	1
	9. Exposure Duration and Frequency	High[A]		1	2	2
	10. Measurement of Test Substance Concentration	Medium	Test concentration was reported in terms of nominal test concentration and was not measured. This study was a limit test and the nominal concentration was far above the limit of solubility.	2	1	2
	11. Number of exposure groups and dose spacing	High	This study was a limit test with one test concentration.	1	1	1
	12. Testing at or Below Solubility Limit	Medium	This study was conducted as a limit test. There was undissolved test material reported in the test vessel.The reported test material solubility was 670 mg/L. This was far higher than the 0.010 mg/L solubility the ECHA Database reported.	2	1	2
Test organisms	13. Test organism characteristics	High	Test organism description was available in Section 4.2 of the study.	1	2	2
	14. Acclimatization and Pretreatment Conditions	High	Ther was a 14 day conditioning period.	1	1	1
	15. Number of Organisms and Replicates per group	High	There were 10 fish/group.	1	1	1
	16. Adequacy of Housing Conditions	High	Aquaria size: 10 litres consisted of glass (length 30 cm, width 22 cm, height 24 cm) and stood in a water bath made from Hostalit ZR with a Plexiglas viewing window.	1	1	1

Outcome assessment	17. Outcome assessment methodology	Medium	Mortality was quantified, but discoloration of the test vessels prevented the observation of sublethal effects.	2	2	4
	18. Consistency of outcome assessment	High	The outcome assessment protocols and results were consistently reported for all test concentrations.	1	1	1
Confounding/ variable control	19. Confounding variables in test setup and procedures	High	There were no reported confounding variables in the experiments that could influence the outcome assessment.	1	2	2
	20. Outcomes unrelated to exposure	High	There were no reported differences among the test groups that could influence the outcome assessment.	1	1	1
Data presentation and analysis	21. Statistical methods	Not Rated	Given that no effects were observed for the one test concentration used in the experiment, no statistics were necessary.	NR	NR	NR
	22. Reporting of data	Medium	Mortality was quantified, but discoloration of the test vessels prevented the observation of sublethal effects.	2	2	4
	23. Explanation of Unexpected Outcomes	Not Rated	There were no unexplained outcomes and no effects observed up to the highest test concentration.	NR	NR	NR
			Sum of scores:	26	29	36
High	Medium	Low	**Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:**	1.241	**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.						

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:	Although the study indicated that this study was conducted according to an internal protocol comparable to OECD Guideline 401, insufficient study details are reported in the study report to verify this.					
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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 and Vehicle 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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not rated* to *Low* .	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 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 (e.g., 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
	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium*	2	2	4
	14. Adequacy and consistency of animal husbandry conditions	Low*	Study provided minimal information on the adequacy of animal husbandry conditions. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	2	2	4
	17. Consistency of outcome assessment	Medium	It is inferred that the 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 variables in test setup and procedures	Medium	Lack of reporting of food/water intake	2	2	4
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine if there were confounding variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Data Presentation and Analysis	23. Statistical methods	Not rated*	Reviewer implied that the investigators did not conduct a statistical analysis. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Not rated* .	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.						

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:	Although the study indicated that this study was conducted according to an internal protocol comparable to OECD Guideline 401, insufficient study details are reported in the study report to verify this.					
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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 and Vehicle 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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not rated* to *Low* .	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 item) was stated, but methods of preparation (e.g., 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 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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium*	2	2	4
	14. Adequacy and consistency of animal husbandry conditions	Low*	Study provided minimal information on the adequacy of animal husbandry conditions. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	3	1	3
	15. Number per group	High		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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	2	2	4
	17. Consistency of outcome assessment	Medium	It is inferred that the 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 variables in test setup and procedures	Medium	Lack of reporting of food/water intake and respiratory rate	2	2	4
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine if there were confounding variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Data Presentation and Analysis	23. Statistical methods	Not rated*	Reviewer implied that the investigators did not conduct a statistical analysis. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Not rated* .	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.						

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 report indicates that the test was conducted according to the OECD TG 401 "Acute Oral Toxicity (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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *Medium* .	2	1	2
Test Setup	4. Negative and Vehicle 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 carrier, 2% starch sludge, but no further details on preparation (e.g., homogeneity of suspension, solubility in starch sludge) or storage of the test substance were reported.	3	1	3
	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 (e.g., 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 onsistency 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

Outcome Assessment	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. Health 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.						

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 ambigously characterized mentioning both vapors and dust. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium*	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 and Vehicle controls	Medium*	The study did not use a vehicle control. The study used a concurrent air control. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not rated* to *Medium* .	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 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 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 (e.g., only nominal concentrations were reported). The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *Unacceptable* .	**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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *Unacceptable* .	**4**	2	8
	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	3	1	3

Exposure Characterization	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. The asterisk (*) indicates that the confidence was reevaluated and changed from Medium to Low.	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 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". The asterisk (*) indicates that the confidence was reevaluated and changed from *HIgh* to *Unacceptable* .	**4**	1	4
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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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 account for the difference. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	2	1	2
Outcome Assessment	16. Outcome assessment methodology	Low*	Significant deficiencies in the reported outcome assessment methodology (i.e., limited information available).The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	2	6
	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 discussed. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3

Outcome Assessment	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	2	1	2
	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	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. The asterisk (*) indicates that the confidence was reevaluated and changed from Not rated to Low.	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	3	2	6
Confounding/ Variable Control	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine whether health outcomes unrelated to exposure affected reported outcomes given the limited information in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
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). The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *Not rated* .	NR	NR	NR
	24. Reporting of data	Low*	Outcome data were minimally provided and discussed. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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):**	**2.9**[1]
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3			**Overall Quality Level:**	**UNACCEPTABLE**[1]

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.

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 ambigously characterized mentioning both vapors and dust. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium*	2	2	4
	2. Test substance source	Low*	No details were provided about the test substance source. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
	3. Test substance purity	Low*	No details were provided about the test substance purity. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Test Setup	4. Negative and Vehicle controls	Unacceptable*	The study did not use a vehicle control. The study used a concurrent air control. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not rated* to *Unacceptable.*	**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 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 (e.g., only nominal concentrations were reported). The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *Unacceptable* .	**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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *Unacceptable* .	**4**	2	8

Exposure Characterization	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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 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 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". The asterisk (*) indicates that the confidence was reevaluated and changed from *HIgh* to *Unacceptable* .	**4**	1	4
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	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Outcome Assessment	16. Outcome assessment methodology	Low*	Significant deficiencies in the reported outcome assessment methodology (i.e., limited information available).The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	2	6
	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 discussed. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3

Outcome Assessment	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). 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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	2	1	2
	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	NR	NR	NR
	20. Negative Control Response	Unacceptable*	The biological responses of the negative control group(s) were not addressed in the study. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not rated* to *Unacceptable* .	**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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	3	2	6
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine whether health outcomes unrelated to exposure affected reported outcomes given the limited information in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from High to Low.	3	1	3
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). The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Not rated* .	NR	NR	NR
	24. Reporting of data	Unacceptable*	Data presentation was inadequate (e.g., the report does not differentiate among findings between air control and treatment groups). The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Unacceptable* .	**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):**	**3.2**[1]
≥1 and <1.7	≥1.7 and <2.3	≥2.3 and ≤3			**Overall Quality Level:**	**UNACCEPTABLE**[1]

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.

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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 and Vehicle 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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not rated* to *Low.*	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
	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 carboxylmethyl cellulose, 21.5%, 46.4% or 50% aqueous suspension) was stated, but the methods of preparation (e.g., 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 (e.g., strain, health status, age).	3	2	6
	14. Adequacy and onsistency of animal husbandry conditions	Low*	Study provided minimal information on the adequacy of animal husbandry conditions. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low*	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	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 variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	3	2	6
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine if there were confounding variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Data Presentation and Analysis	23. Statistical methods	Not rated*	Reviewer implied that the investigators did not conduct a statistical analysis. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Not rated* .	NR	NR	NR
	24. Reporting of data	Low*	Outcome data were minimally provided and discussed. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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.						

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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 and Vehicle 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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Not rated* to *Low* .	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
	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 carboxylmethyl cellulose, 46.4% or 50% aqueous suspension) was stated, but the methods of preparation (e.g., 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 (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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low*	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	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 variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	3	2	6
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine if there were confounding variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Data Presentation and Analysis	23. Statistical methods	Not rated*	Reviewer implied that the investigators did not conduct a statistical analysis. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Not rated* .	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:	**45.0**	**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.						

Study Reference:	Stark, D., Treumann, S., van Ravenzwaay, B. 2013. Reproduction/developmental Toxicity Screening Test in 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[A]	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[A]	Test item was received by the submitter and the batch number was provided.	1	1	1
	3. Test substance purity	High[A]	Purity was characterized in the appendix of the study.	1	1	1
Test Setup	4. Negative and Vehicle 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
	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 onsistency 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

Outcome Assessment	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. Health outcomes unrelated to exposure	High[A]		1	1	1
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.						

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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 and Vehicle 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 randomization was not required. The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *Not rated* .	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 (e.g., 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 (e.g., 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	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	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.e., limited information). The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low.*	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.The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	NR	NR	NR
	20. Negative Control Response	Not rated*	Negative controls were not required for the study. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	NR	NR	NR
Confounding/ Variable Control	21. Confounding variables in test setup and procedures	Medium	Initial food/water intakewere not reported but this is not likely to have a significant impact on results.	2	2	4
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine if there were confounding variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Data Presentation and Analysis	23. Statistical methods	Not rated*	Reviewer implied that the investigators did not conduct a statistical analysis. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Not rated* .	NR	NR	NR
	24. Reporting of data	High*	Dermal responses were reported for both female rabbits at different timepoints. The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *High* .	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.						

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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 and Vehicle 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 randomization was not required. Note that the original qualitative determination was *Low* . It has been changed to *Not rated* .	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 (e.g., 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 (e.g., 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 onsistency of animal husbandry conditions	Medium	Study provided minimal information on the adequacy of animal husbandry conditions.	2	1	2
	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.e., limited information). The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low*	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	NR	NR	NR
	20. Negative Control Response	Not rated*	Negative controls were not required for the study. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	NR	NR	NR
Confounding/ Variable Control	21. Confounding variables in test setup and procedures	Medium	Initial food/water intakewere not reported but this is not likely to have a significant impact on results.	2	2	4
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine if there were confounding variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Data Presentation and Analysis	23. Statistical methods	Not rated*	Reviewer implied that the investigators did not conduct a statistical analysis. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Not rated* .	NR	NR	NR
	24. Reporting of data	High*	Dermal responses were reported for male and female rabbits at different timepoints. The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *High* .	1	2	2
			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.						

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 and Vehicle 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 0.3ml of 0.9% Nacl solution. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
	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 onsistency 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

Outcome Assessment	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.The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Not rated* .	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 and respiratory rate were not reported but this is not likely to have a significant impact on results.The asterisk (*) indicates that the confidence was reevaluated and changed from *High* To *Medium* .	2	2	4
	22. Health 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.

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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High to Medium* .	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 and Vehicle 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
	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 oneo f 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 (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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Low* to *Medium* .	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 (e.g., criteria for study termination). The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 same method based on details provided in the study. However, the study did not address the measures that the investigators put in place (e.g., training of staff in scoring) to have consistency in the outcome assessment. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	2	1	2
	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 occular 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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	2	6
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine if there were confounding variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	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 control and treated eyes in both female rabbits.	1	2	2
			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.						

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					
Notes	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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	2	2	4
	2. Test substance source	Low*	No details were provided about the source and lot number of the test substance.The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
	3. Test substance purity	Low*	No details were provided about the test substance purity. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	1	3
Test Setup	4. Negative and Vehicle 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
	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 (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. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	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 (e.g., criteria for study termination). The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 same method based on details provided in the study. However, the study did not address the measures that the investigators put in place (e.g., training of staff in scoring) to have consistency in the outcome assessment.he asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	2	1	2
	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 occular 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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	3	2	6
	22. Health outcomes unrelated to exposure	Low*	It is not possible to determine if there were confounding variables with the limited information given in the report. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	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 control and treated eyes in male rabbits. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Low* .	1	2	2
			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.						

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 and Vehicle 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 time-frame between formulation 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 soultion. The asterisk (*) indicates that the confidence was reevaluated and changed from *Medium* to *Low* .	3	1	3
	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 onsistency 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

Outcome Assessment	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. Health 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.						

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 substance in propylene glycol were not reported.	2	1	2
	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 fi 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 wee 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 onsistency of animal husbandry conditions	High	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 intrest and was sensitive for the outcome of interest.	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	1	1

Outcome Assessment	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 adquate	1	1	1
Confounding/ Variable Control	21. Confounding variables in test setup and procedures	High[A]		1	2	2
	22. Health 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 statsticaly analysis was not required as the test substance did not cause significant change	1	1	1
	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.						

Study Reference:	Jung, R., Weigand, W. 1983. Perylimid Study of the Mutagenic Potential in Strains of Salmonella Typhimurium (Ames Test) and Escherichia coli. Hoechst Aktiengesellschaft, Germany. Report No. 83.0695. For Hoechst, Farbenforschung, 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 procedures	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 was not provided. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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	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 Salmonella typhimurium was choosed 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
Outcome Assessment	16. Outcome assessment methodology	High	The outcome assessment methology 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

Outcome Assessment	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[A]	Statastical methods, calculation and methods were not required	1	1	1
	23. Data interpretation	High[A]	Evaluation criteria appreated to be limited to positive controls, defined as a significant increase in revertant colonies	1	2	2
	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.						

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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 procedures	High[A]		1	1	1
	7. Standards for test	High	Mutant colonies per 106 cell identified in solvent control should be within the laboratory historical controls and positive control substance is expected to produce significant increase in mutant colony frequency.	1	1	1
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. The asterisk (*) indicates that the confidence was reevaluated and changed from *High* to *Medium* .	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 choosed 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. Th enumber of replicates/concentration was appropriate	1	1	1

Outcome Assessment	16. Outcome assessment methodology	High	The outcome assessment methology 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	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	Statastical methods, calculation and methods were presented	1	1	1
	23. Data interpretation	High	Evaluation criteria appreated 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 mutagenicity test, so this metric is not applicable	NR	NR	NR
	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.