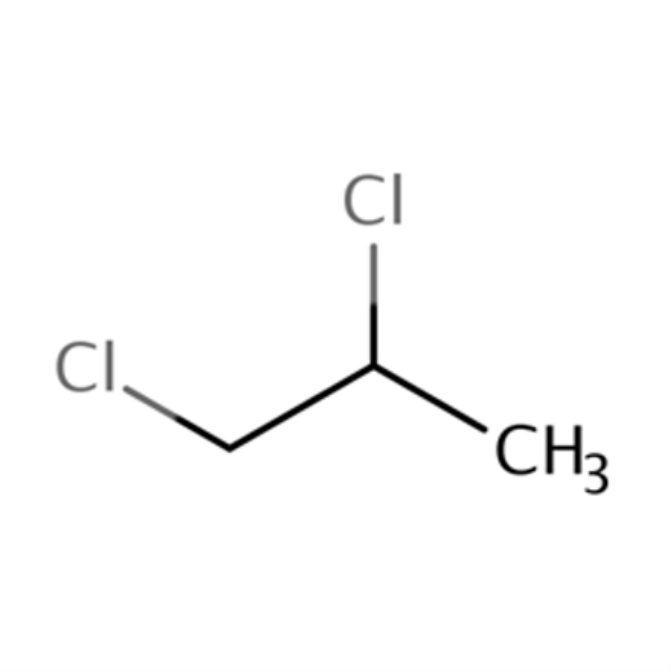
United States
Environmental Protection Agency

May 2026
Office of Chemical Safety and
Pollution Prevention

Draft Data Quality Evaluation Information for Dermal Absorption for 1,2-Dichloropropane

Systematic Review Support Document for the Draft Risk Evaluation

CASRN: 78-87-5



May 2026

This supplemental file contains information regarding the data evaluation results for data sources that met the PECO screening criteria for the *Draft Risk Evaluation for 1,2-Dichloropropane* and were used to characterize dermal absorption. EPA conducted data quality evaluation based on author-reported descriptions and results; additional analyses (*e.g.*, statistical analyses performed during data integration into the risk evaluation) potentially conducted by EPA are not contained in this supplemental file. Key parameters and corresponding data for each condition were not extracted from the reference. EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (also referred to as the '2021 Draft Systematic Review Protocol'). Any updated steps in the systematic review process since the publication of the 2021 Draft Systematic Review Protocol are described in the *Draft Systematic Review Protocol for 1,2-Dichloropropane*.

To evaluate dermal absorption references, EPA consulted several OECD documents when considering quality rankings for individual metrics. Each condition (*e.g.*, individual concentrations tested or different experimental designs) is evaluated independently within a given reference, therefore each reference may have more than one overall quality determination (OQD) to more appropriately reflect the quality of each condition. No OQD is determined for each reference as a whole, if it contains data from more than one condition. A single reference may evaluate only a limited number of conditions (*e.g.*, use of only the neat compound). If all other methods and results are adequate, the study may be considered acceptable for certain conditions of use. However, the study may still be limited for use in the risk evaluation because it may not address other uses (*e.g.*, lower concentrations, certain solvents/diluents).

Table of Contents

Study Citation:	Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID:	Finite; Neat

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number:78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of prepared solutions were determined by study authors using HPLC prior to application; all were ≥93.3% and ≤96.2%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) was used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; Neat

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	High	Assay methods and procedures were appropriately described. This study was conducted according to OECD TG 428, and OECD 28. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was monitored, but the results were not reported. Finite doses of 1,2-dichloropropane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates [4 donors]; surface area of 0.64 cm2). Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and was dermatomed (thickness ranged from 360 to 400 um). The test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747). The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300 uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. Skin washed at 8 hours and 24 hours post-dose with dilute soap solution (2% v/v total of 5 ml) and dried with tissue swaps. The carbon filter and pouch of Anasorb 747 were collected at 2, 8 and 24 hours post-dose. The skin was tape-stripped 20 times and analyzed. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms although threshold values of 5 kilo-ohms for human skin may also be appropriate (Brackin et al. 2024 [Toxiol. In Vitro 95:105735]. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. Coefficients of variation (CV) values were not reported but could be calculated. Further discussion of the CVs is provided in Metric 19. The mass balance was 90.92% (neat), 88.74% (50% in IPM) and 89.17% (10% in IPM), 88.89% (1% in IPM), 91.77% (50% in kerosene), 102.02 (10% in kerosene), and 101.95% (1% in kerosene); which are acceptable for this volatile chemical.

Domain 3: Exposure Characterization

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; Neat

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparations of the test solutions were adequately reported. The volumes of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (10 uL/cm2) and volume (6.4 uL) were delivered consistently across study groups to exposed skin. This is in agreement with OECD guidelines. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered a minor difference and acceptable.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration was reported and appropriate for determining absorption. The test substance was in contact with the skin for 8 hours prior to washing. Samples of receptor fluid were collected for a total of 24 hours.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 4 dose groups tested in a wide range of concentrations (neat, 50%, 10%, and 1%). Dilutions of test substance was performed in two different vehicles (isopropyl myristate and kerosene). Justification for dose selection was provided by authors as realistic operator exposures.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. An application rate of 10 uL/cm2 was applied to skin samples. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; Neat

Domain	Metric		Rating	Comments
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assessed consistently across study replicates. The same duration of exposure, receptor fluid used, and the sampling period were consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of $>$17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were presented across a time series. The CVs for the total absorbed dose were $>$25 % for all doses tested; however, sufficient data are provided for EPA to calculate an alternate (upper-end) value to account for variability in the results.
	Metric 20:	Data interpretation	Medium	Recovery of the applied test substance was adequate given its volatility ($>$88.74%). The study performed 20 tape strippings; all 20 were categorized as stratum corneum and analyzed together. The ”total absorbed dose” was based on the amount of test substance in the receptor fluid and the receptor chamber wash and did not include the skin compartment. However, the study did report a ”dermal delivery” value that included the absorbed dose + exposed skin. Tape strips were not included in either calculation; however, sufficient data are available to allow for an independent analysis.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means $\pm$ SD. Individual replicate data were provided.

Overall Quality Determination High

Continued on next page . . .

. . . continued from previous page

Study Citation:	Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID:	Finite; Neat

Domain	Metric	Rating	Comments

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 50% in IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number:78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of prepared solutions were determined by study authors using HPLC prior to application; all were $\geq$93.3% and $\leq$96.2%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) was used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.

Continued on next page ...

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 50% in IPM

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	High	Assay methods and procedures were appropriately described. This study was conducted according to OECD TG 428, and OECD 28. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was monitored, but the results were not reported. Finite doses of 1,2-dichloropropane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates [4 donors]; surface area of 0.64 cm2). Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and was dermatomed (thickness ranged from 360 to 400 um). The test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747). The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300 uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. Skin washed at 8 hours and 24 hours post-dose with dilute soap solution (2% v/v total of 5 ml) and dried with tissue swaps. The carbon filter and pouch of Anasorb 747 were collected at 2, 8 and 24 hours post-dose. The skin was tape-stripped 20 times and analyzed. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms although threshold values of 5 kilo-ohms for human skin may also be appropriate (Brackin et al. 2024 [Toxiol. In Vitro 95:105735]. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. Coefficients of variation (CV) values were not reported but could be calculated. Further discussion of the CVs is provided in Metric 19. The mass balance was 90.92% (neat), 88.74% (50% in IPM) and 89.17% (10% in IPM), 88.89% (1% in IPM), 91.77% (50% in kerosene), 102.02 (10% in kerosene), and 101.95% (1% in kerosene); which are acceptable for this volatile chemical.

Domain 3: Exposure Characterization

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 50% in IPM

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparations of the test solutions were adequately reported. The volumes of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (10 uL/cm2) and volume (6.4 uL) were delivered consistently across study groups to exposed skin. This is in agreement with OECD guidelines. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered a minor difference and acceptable.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration was reported and appropriate for determining absorption. The test substance was in contact with the skin for 8 hours prior to washing. Samples of receptor fluid were collected for a total of 24 hours.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 4 dose groups tested in a wide range of concentrations (neat, 50%, 10%, and 1%). Dilutions of test substance was performed in two different vehicles (isopropyl myristate and kerosene). Justification for dose selection was provided by authors as realistic operator exposures.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. An application rate of 10 uL/cm2 was applied to skin samples. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 50% in IPM

Domain	Metric		Rating	Comments
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assessed consistently across study replicates. The same duration of exposure, receptor fluid used, and the sampling period were consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of $>$17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were presented across a time series. The CVs for the total absorbed dose were $>$25 % for all doses tested; however, sufficient data are provided for EPA to calculate an alternate (upper-end) value to account for variability in the results.
	Metric 20:	Data interpretation	Medium	Recovery of the applied test substance was adequate given its volatility ($>$88.74%). The study performed 20 tape strippings; all 20 were categorized as stratum corneum and analyzed together. The ”total absorbed dose” was based on the amount of test substance in the receptor fluid and the receptor chamber wash and did not include the skin compartment. However, the study did report a ”dermal delivery” value that included the absorbed dose + exposed skin. Tape strips were not included in either calculation; however, sufficient data are available to allow for an independent analysis.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means $\pm$ SD. Individual replicate data were provided.

Overall Quality Determination — High

Continued on next page . . .

. . . continued from previous page

Study Citation:	Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID:	Finite; 50% in IPM

Domain	Metric	Rating	Comments

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 10% in IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number:78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of prepared solutions were determined by study authors using HPLC prior to application; all were $\geq$93.3% and $\leq$96.2%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) was used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 10% in IPM

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	High	Assay methods and procedures were appropriately described. This study was conducted according to OECD TG 428, and OECD 28. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was monitored, but the results were not reported. Finite doses of 1,2-dichloropropane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates [4 donors]; surface area of 0.64 cm2). Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and was dermatomed (thickness ranged from 360 to 400 um). The test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747). The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300 uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. Skin washed at 8 hours and 24 hours post-dose with dilute soap solution (2% v/v total of 5 ml) and dried with tissue swaps. The carbon filter and pouch of Anasorb 747 were collected at 2, 8 and 24 hours post-dose. The skin was tape-stripped 20 times and analyzed. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms although threshold values of 5 kilo-ohms for human skin may also be appropriate (Brackin et al. 2024 [Toxiol. In Vitro 95:105735]. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. Coefficients of variation (CV) values were not reported but could be calculated. Further discussion of the CVs is provided in Metric 19. The mass balance was 90.92% (neat), 88.74% (50% in IPM) and 89.17% (10% in IPM), 88.89% (1% in IPM), 91.77% (50% in kerosene), 102.02 (10% in kerosene), and 101.95% (1% in kerosene); which are acceptable for this volatile chemical.

Domain 3: Exposure Characterization

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 10% in IPM

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparations of the test solutions were adequately reported. The volumes of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (10 uL/cm2) and volume (6.4 uL) were delivered consistently across study groups to exposed skin. This is in agreement with OECD guidelines. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered a minor difference and acceptable.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration was reported and appropriate for determining absorption. The test substance was in contact with the skin for 8 hours prior to washing. Samples of receptor fluid were collected for a total of 24 hours.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 4 dose groups tested in a wide range of concentrations (neat, 50%, 10%, and 1%). Dilutions of test substance was performed in two different vehicles (isopropyl myristate and kerosene). Justification for dose selection was provided by authors as realistic operator exposures.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. An application rate of 10 uL/cm2 was applied to skin samples. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 10% in IPM

Domain	Metric		Rating	Comments
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assessed consistently across study replicates. The same duration of exposure, receptor fluid used, and the sampling period were consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of $>$17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were presented across a time series. The CVs for the total absorbed dose were $>$25 % for all doses tested; however, sufficient data are provided for EPA to calculate an alternate (upper-end) value to account for variability in the results.
	Metric 20:	Data interpretation	Medium	Recovery of the applied test substance was adequate given its volatility ($>$88.74%). The study performed 20 tape strippings; all 20 were categorized as stratum corneum and analyzed together. The ”total absorbed dose” was based on the amount of test substance in the receptor fluid and the receptor chamber wash and did not include the skin compartment. However, the study did report a ”dermal delivery” value that included the absorbed dose + exposed skin. Tape strips were not included in either calculation; however, sufficient data are available to allow for an independent analysis.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means $\pm$ SD. Individual replicate data were provided.

Overall Quality Determination — High

Continued on next page . . .

. . . continued from previous page

Study Citation:	Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID:	Finite; 10% in IPM

Domain	Metric	Rating	Comments

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 1% in IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number:78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of prepared solutions were determined by study authors using HPLC prior to application; all were $\geq$93.3% and $\leq$96.2%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) was used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 1% in IPM

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	High	Assay methods and procedures were appropriately described. This study was conducted according to OECD TG 428, and OECD 28. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was monitored, but the results were not reported. Finite doses of 1,2-dichloropropane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates [4 donors]; surface area of 0.64 cm2). Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and was dermatomed (thickness ranged from 360 to 400 um). The test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747). The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300 uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. Skin washed at 8 hours and 24 hours post-dose with dilute soap solution (2% v/v total of 5 ml) and dried with tissue swaps. The carbon filter and pouch of Anasorb 747 were collected at 2, 8 and 24 hours post-dose. The skin was tape-stripped 20 times and analyzed. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms although threshold values of 5 kilo-ohms for human skin may also be appropriate (Brackin et al. 2024 [Toxiol. In Vitro 95:105735]. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. Coefficients of variation (CV) values were not reported but could be calculated. Further discussion of the CVs is provided in Metric 19. The mass balance was 90.92% (neat), 88.74% (50% in IPM) and 89.17% (10% in IPM), 88.89% (1% in IPM), 91.77% (50% in kerosene), 102.02 (10% in kerosene), and 101.95% (1% in kerosene); which are acceptable for this volatile chemical.

Domain 3: Exposure Characterization

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 1% in IPM

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparations of the test solutions were adequately reported. The volumes of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (10 uL/cm2) and volume (6.4 uL) were delivered consistently across study groups to exposed skin. This is in agreement with OECD guidelines. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered a minor difference and acceptable.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration was reported and appropriate for determining absorption. The test substance was in contact with the skin for 8 hours prior to washing. Samples of receptor fluid were collected for a total of 24 hours.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 4 dose groups tested in a wide range of concentrations (neat, 50%, 10%, and 1%). Dilutions of test substance was performed in two different vehicles (isopropyl myristate and kerosene). Justification for dose selection was provided by authors as realistic operator exposures.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. An application rate of 10 uL/cm2 was applied to skin samples. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 1% in IPM

Domain	Metric		Rating	Comments
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assessed consistently across study replicates. The same duration of exposure, receptor fluid used, and the sampling period were consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of $>$17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were presented across a time series. The CVs for the total absorbed dose were $>$25 % for all doses tested; however, sufficient data are provided for EPA to calculate an alternate (upper-end) value to account for variability in the results.
	Metric 20:	Data interpretation	Medium	Recovery of the applied test substance was adequate given its volatility ($>$88.74%). The study performed 20 tape strippings; all 20 were categorized as stratum corneum and analyzed together. The ”total absorbed dose” was based on the amount of test substance in the receptor fluid and the receptor chamber wash and did not include the skin compartment. However, the study did report a ”dermal delivery” value that included the absorbed dose + exposed skin. Tape strips were not included in either calculation; however, sufficient data are available to allow for an independent analysis.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means $\pm$ SD. Individual replicate data were provided.

Overall Quality Determination — High

Continued on next page . . .

. . . continued from previous page

Study Citation:	Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID:	Finite; 1% in IPM

Domain	Metric	Rating	Comments

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 50% in Kerosene

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number:78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of prepared solutions were determined by study authors using HPLC prior to application; all were ≥93.3% and ≤96.2%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) was used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 50% in Kerosene

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	High	Assay methods and procedures were appropriately described. This study was conducted according to OECD TG 428, and OECD 28. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was monitored, but the results were not reported. Finite doses of 1,2-dichloropropane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates [4 donors]; surface area of 0.64 cm2). Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and was dermatomed (thickness ranged from 360 to 400 um). The test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747). The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300 uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. Skin washed at 8 hours and 24 hours post-dose with dilute soap solution (2% v/v total of 5 ml) and dried with tissue swaps. The carbon filter and pouch of Anasorb 747 were collected at 2, 8 and 24 hours post-dose. The skin was tape-stripped 20 times and analyzed. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms although threshold values of 5 kilo-ohms for human skin may also be appropriate (Brackin et al. 2024 [Toxiol. In Vitro 95:105735]. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. Coefficients of variation (CV) values were not reported but could be calculated. Further discussion of the CVs is provided in Metric 19. The mass balance was 90.92% (neat), 88.74% (50% in IPM) and 89.17% (10% in IPM), 88.89% (1% in IPM), 91.77% (50% in kerosene), 102.02 (10% in kerosene), and 101.95% (1% in kerosene); which are acceptable for this volatile chemical.

Domain 3: Exposure Characterization

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 50% in Kerosene

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparations of the test solutions were adequately reported. The volumes of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (10 uL/cm2) and volume (6.4 uL) were delivered consistently across study groups to exposed skin. This is in agreement with OECD guidelines. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered a minor difference and acceptable.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration was reported and appropriate for determining absorption. The test substance was in contact with the skin for 8 hours prior to washing. Samples of receptor fluid were collected for a total of 24 hours.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 4 dose groups tested in a wide range of concentrations (neat, 50%, 10%, and 1%). Dilutions of test substance was performed in two different vehicles (isopropyl myristate and kerosene). Justification for dose selection was provided by authors as realistic operator exposures.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. An application rate of 10 uL/cm2 was applied to skin samples. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 50% in Kerosene

Domain	Metric		Rating	Comments
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assessed consistently across study replicates. The same duration of exposure, receptor fluid used, and the sampling period were consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of $>$17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were presented across a time series. The CVs for the total absorbed dose were $>$25 % for all doses tested; however, sufficient data are provided for EPA to calculate an alternate (upper-end) value to account for variability in the results.
	Metric 20:	Data interpretation	Medium	Recovery of the applied test substance was adequate given its volatility ($>$88.74%). The study performed 20 tape strippings; all 20 were categorized as stratum corneum and analyzed together. The ”total absorbed dose” was based on the amount of test substance in the receptor fluid and the receptor chamber wash and did not include the skin compartment. However, the study did report a ”dermal delivery” value that included the absorbed dose + exposed skin. Tape strips were not included in either calculation; however, sufficient data are available to allow for an independent analysis.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means $\pm$ SD. Individual replicate data were provided.

Overall Quality Determination — High

Continued on next page . . .

. . . continued from previous page

Study Citation:	Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID:	Finite; 50% in Kerosene

Domain	Metric	Rating	Comments

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 10% in Kerosene

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number:78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of prepared solutions were determined by study authors using HPLC prior to application; all were $\geq$93.3% and $\leq$96.2%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) was used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 10% in Kerosene

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	High	Assay methods and procedures were appropriately described. This study was conducted according to OECD TG 428, and OECD 28. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was monitored, but the results were not reported. Finite doses of 1,2-dichloropropane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates [4 donors]; surface area of 0.64 cm2). Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and was dermatomed (thickness ranged from 360 to 400 um). The test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747). The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300 uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. Skin washed at 8 hours and 24 hours post-dose with dilute soap solution (2% v/v total of 5 ml) and dried with tissue swaps. The carbon filter and pouch of Anasorb 747 were collected at 2, 8 and 24 hours post-dose. The skin was tape-stripped 20 times and analyzed. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms although threshold values of 5 kilo-ohms for human skin may also be appropriate (Brackin et al. 2024 [Toxiol. In Vitro 95:105735]. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. Coefficients of variation (CV) values were not reported but could be calculated. Further discussion of the CVs is provided in Metric 19. The mass balance was 90.92% (neat), 88.74% (50% in IPM) and 89.17% (10% in IPM), 88.89% (1% in IPM), 91.77% (50% in kerosene), 102.02 (10% in kerosene), and 101.95% (1% in kerosene); which are acceptable for this volatile chemical.

Domain 3: Exposure Characterization

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 10% in Kerosene

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparations of the test solutions were adequately reported. The volumes of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (10 uL/cm2) and volume (6.4 uL) were delivered consistently across study groups to exposed skin. This is in agreement with OECD guidelines. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered a minor difference and acceptable.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration was reported and appropriate for determining absorption. The test substance was in contact with the skin for 8 hours prior to washing. Samples of receptor fluid were collected for a total of 24 hours.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 4 dose groups tested in a wide range of concentrations (neat, 50%, 10%, and 1%). Dilutions of test substance was performed in two different vehicles (isopropyl myristate and kerosene). Justification for dose selection was provided by authors as realistic operator exposures.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. An application rate of 10 uL/cm2 was applied to skin samples. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 10% in Kerosene

Domain	Metric		Rating	Comments
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assessed consistently across study replicates. The same duration of exposure, receptor fluid used, and the sampling period were consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of $>$17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were presented across a time series. The CVs for the total absorbed dose were $>$25 % for all doses tested; however, sufficient data are provided for EPA to calculate an alternate (upper-end) value to account for variability in the results.
	Metric 20:	Data interpretation	Medium	Recovery of the applied test substance was adequate given its volatility ($>$88.74%). The study performed 20 tape strippings; all 20 were categorized as stratum corneum and analyzed together. The ”total absorbed dose” was based on the amount of test substance in the receptor fluid and the receptor chamber wash and did not include the skin compartment. However, the study did report a ”dermal delivery” value that included the absorbed dose + exposed skin. Tape strips were not included in either calculation; however, sufficient data are available to allow for an independent analysis.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means $\pm$ SD. Individual replicate data were provided.

Overall Quality Determination — High

Continued on next page . . .

. . . continued from previous page

Study Citation:	Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID:	Finite; 10% in Kerosene

Domain	Metric	Rating	Comments

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 1% in Kerosene

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number:78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of prepared solutions were determined by study authors using HPLC prior to application; all were ≥93.3% and ≤96.2%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) was used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 1% in Kerosene

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	High	Assay methods and procedures were appropriately described. This study was conducted according to OECD TG 428, and OECD 28. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was monitored, but the results were not reported. Finite doses of 1,2-dichloropropane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates [4 donors]; surface area of 0.64 cm2). Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and was dermatomed (thickness ranged from 360 to 400 um). The test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747). The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300 uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. Skin washed at 8 hours and 24 hours post-dose with dilute soap solution (2% v/v total of 5 ml) and dried with tissue swaps. The carbon filter and pouch of Anasorb 747 were collected at 2, 8 and 24 hours post-dose. The skin was tape-stripped 20 times and analyzed. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms although threshold values of 5 kilo-ohms for human skin may also be appropriate (Brackin et al. 2024 [Toxiol. In Vitro 95:105735]. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. Coefficients of variation (CV) values were not reported but could be calculated. Further discussion of the CVs is provided in Metric 19. The mass balance was 90.92% (neat), 88.74% (50% in IPM) and 89.17% (10% in IPM), 88.89% (1% in IPM), 91.77% (50% in kerosene), 102.02 (10% in kerosene), and 101.95% (1% in kerosene); which are acceptable for this volatile chemical.

Domain 3: Exposure Characterization

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 1% in Kerosene

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparations of the test solutions were adequately reported. The volumes of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (10 uL/cm2) and volume (6.4 uL) were delivered consistently across study groups to exposed skin. This is in agreement with OECD guidelines. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered a minor difference and acceptable.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration was reported and appropriate for determining absorption. The test substance was in contact with the skin for 8 hours prior to washing. Samples of receptor fluid were collected for a total of 24 hours.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 4 dose groups tested in a wide range of concentrations (neat, 50%, 10%, and 1%). Dilutions of test substance was performed in two different vehicles (isopropyl myristate and kerosene). Justification for dose selection was provided by authors as realistic operator exposures.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. An application rate of 10 uL/cm2 was applied to skin samples. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Finite; 1% in Kerosene

Domain	Metric		Rating	Comments
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assessed consistently across study replicates. The same duration of exposure, receptor fluid used, and the sampling period were consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of $>$17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were presented across a time series. The CVs for the total absorbed dose were $>$25 % for all doses tested; however, sufficient data are provided for EPA to calculate an alternate (upper-end) value to account for variability in the results.
	Metric 20:	Data interpretation	Medium	Recovery of the applied test substance was adequate given its volatility ($>$88.74%). The study performed 20 tape strippings; all 20 were categorized as stratum corneum and analyzed together. The "total absorbed dose" was based on the amount of test substance in the receptor fluid and the receptor chamber wash and did not include the skin compartment. However, the study did report a "dermal delivery" value that included the absorbed dose + exposed skin. Tape strips were not included in either calculation; however, sufficient data are available to allow for an independent analysis.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means $\pm$ SD. Individual replicate data were provided.

Overall Quality Determination — High

Continued on next page . . .

. . . continued from previous page

Study Citation:	Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID:	Finite; 1% in Kerosene

Domain	Metric	Rating	Comments

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; Neat

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number: 78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	High	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of the prepared solution were determined by study authors using HPLC prior to application; all were ≥92.5%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) were used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report the mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.
	Metric 5:	Assay procedures	High	This study was conducted according to OECD TG 428, and OECD 28. The assay procedures specified in the report were described in detail, although some information was missing. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was not reported but was monitored. Infinite doses of 1,2-dichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates; surface area of 0.64 cm2). The volume applied (640 uL) was necessary to achieve the desired application rate of 1000 uL/cm2. Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and dermatomed (thickness ranged from 360 to 400 um). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747) for 24 hours. The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. An equal volume was replaced. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”. A steady state was reached.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; Neat

Domain	Metric		Rating	Comments
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. The percentage of the recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. The study did report a cumulative absorption in the receptor fluid at each time point. Coefficients of variation (CV) values were not reported for Kp, but could be calculated for cumulative absorption.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of the test substance was adequately reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (1000 uL/cm2) and volume (64 uL) were delivered consistently across study groups to exposed skin. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered to be minor and unlikely to have an impact on the study results.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and appropriate for Kp determination. A steady state flux was obtained.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 3 dose groups tested in a wide range of concentrations (neat, 50%, and 10%). Dilutions of the test substance were performed in two different vehicles (isopropyl myristate or kerosene). The authors provided justification for the application rate (1000 uL/cm2), chosen to establish a non-depletable dose, and doses, as realistic operator exposures.
Domain 4: Test Model				

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; Neat

Domain	Metric		Rating	Comments
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. Measurement techniques and timing were reported and appropriate. An infinite dose of the test substance was used to determine the Kp. An application rate of 1000 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2.
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assess consistently across study replicates. The same duration of exposure, receptor fluid used, and sampling period was consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of >17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; Neat

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported for the cumulative amount of test substance in the receptor fluid at each time point. Mathematical calculations used to determine Kp were reported. The Kp was correctly based on the linear data phase of the absorption curve. CV values were not reported for Kp and could not be determined.
	Metric 20:	Data interpretation	High	The Kp values were derived from an appropriate exposure condition (infinite dose). Recovery was not reported but this determination is not relevant for infinite dose applications. Kps were calculated from the linear portion of the absorption curve.
	Metric 21:	Reporting of data	Medium	Data for cumulative absorption for each time point and cell were reported. Data were also reported as means ± SD. Calculated Kp were not reported with SD or CV.

Overall Quality Determination High

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 50% in IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number: 78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	High	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of the prepared solution were determined by study authors using HPLC prior to application; all were ≥92.5%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) were used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report the mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.
	Metric 5:	Assay procedures	High	This study was conducted according to OECD TG 428, and OECD 28. The assay procedures specified in the report were described in detail, although some information was missing. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was not reported but was monitored. Infinite doses of 1,2-dichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates; surface area of 0.64 cm2). The volume applied (640 uL) was necessary to achieve the desired application rate of 1000 uL/cm2. Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and dermatomed (thickness ranged from 360 to 400 um). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747) for 24 hours. The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. An equal volume was replaced. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”. A steady state was reached.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 50% in IPM

Domain	Metric		Rating	Comments
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. The percentage of the recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. The study did report a cumulative absorption in the receptor fluid at each time point. Coefficients of variation (CV) values were not reported for Kp, but could be calculated for cumulative absorption.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of the test substance was adequately reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (1000 uL/cm2) and volume (64 uL) were delivered consistently across study groups to exposed skin. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered to be minor and unlikely to have an impact on the study results.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and appropriate for Kp determination. A steady state flux was obtained.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 3 dose groups tested in a wide range of concentrations (neat, 50%, and 10%). Dilutions of the test substance were performed in two different vehicles (isopropyl myristate or kerosene). The authors provided justification for the application rate (1000 uL/cm2), chosen to establish a non-depletable dose, and doses, as realistic operator exposures.
Domain 4: Test Model				

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 50% in IPM

Domain	Metric		Rating	Comments
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. Measurement techniques and timing were reported and appropriate. An infinite dose of the test substance was used to determine the Kp. An application rate of 1000 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2.
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assess consistently across study replicates. The same duration of exposure, receptor fluid used, and sampling period was consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of >17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 50% in IPM

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported for the cumulative amount of test substance in the receptor fluid at each time point. Mathematical calculations used to determine Kp were reported. The Kp was correctly based on the linear data phase of the absorption curve. CV values were not reported for Kp and could not be determined.
	Metric 20:	Data interpretation	High	The Kp values were derived from an appropriate exposure condition (infinite dose). Recovery was not reported but this determination is not relevant for infinite dose applications. Kps were calculated from the linear portion of the absorption curve.
	Metric 21:	Reporting of data	Medium	Data for cumulative absorption for each time point and cell were reported. Data were also reported as means ± SD. Calculated Kp were not reported with SD or CV.

Overall Quality Determination — High

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 10% in IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number: 78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	High	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of the prepared solution were determined by study authors using HPLC prior to application; all were ≥92.5%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) were used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report the mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.
	Metric 5:	Assay procedures	High	This study was conducted according to OECD TG 428, and OECD 28. The assay procedures specified in the report were described in detail, although some information was missing. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was not reported but was monitored. Infinite doses of 1,2-dichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates; surface area of 0.64 cm2). The volume applied (640 uL) was necessary to achieve the desired application rate of 1000 uL/cm2. Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and dermatomed (thickness ranged from 360 to 400 um). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747) for 24 hours. The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. An equal volume was replaced. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”. A steady state was reached.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 10% in IPM

Domain	Metric		Rating	Comments
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. The percentage of the recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. The study did report a cumulative absorption in the receptor fluid at each time point. Coefficients of variation (CV) values were not reported for Kp, but could be calculated for cumulative absorption.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of the test substance was adequately reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (1000 uL/cm2) and volume (64 uL) were delivered consistently across study groups to exposed skin. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered to be minor and unlikely to have an impact on the study results.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and appropriate for Kp determination. A steady state flux was obtained.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 3 dose groups tested in a wide range of concentrations (neat, 50%, and 10%). Dilutions of the test substance were performed in two different vehicles (isopropyl myristate or kerosene). The authors provided justification for the application rate (1000 uL/cm2), chosen to establish a non-depletable dose, and doses, as realistic operator exposures.
Domain 4: Test Model				

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 10% in IPM

Domain	Metric		Rating	Comments
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. Measurement techniques and timing were reported and appropriate. An infinite dose of the test substance was used to determine the Kp. An application rate of 1000 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2.
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assess consistently across study replicates. The same duration of exposure, receptor fluid used, and sampling period was consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of >17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 10% in IPM

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported for the cumulative amount of test substance in the receptor fluid at each time point. Mathematical calculations used to determine Kp were reported. The Kp was correctly based on the linear data phase of the absorption curve. CV values were not reported for Kp and could not be determined.
	Metric 20:	Data interpretation	High	The Kp values were derived from an appropriate exposure condition (infinite dose). Recovery was not reported but this determination is not relevant for infinite dose applications. Kps were calculated from the linear portion of the absorption curve.
	Metric 21:	Reporting of data	Medium	Data for cumulative absorption for each time point and cell were reported. Data were also reported as means ± SD. Calculated Kp were not reported with SD or CV.

Overall Quality Determination High

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 50% in kerosene

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number: 78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	High	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of the prepared solution were determined by study authors using HPLC prior to application; all were ≥92.5%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) were used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report the mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.
	Metric 5:	Assay procedures	High	This study was conducted according to OECD TG 428, and OECD 28. The assay procedures specified in the report were described in detail, although some information was missing. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was not reported but was monitored. Infinite doses of 1,2-dichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates; surface area of 0.64 cm2). The volume applied (640 uL) was necessary to achieve the desired application rate of 1000 uL/cm2. Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and dermatomed (thickness ranged from 360 to 400 um). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747) for 24 hours. The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. An equal volume was replaced. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”. A steady state was reached.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 50% in kerosene

Domain	Metric		Rating	Comments
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. The percentage of the recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. The study did report a cumulative absorption in the receptor fluid at each time point. Coefficients of variation (CV) values were not reported for Kp, but could be calculated for cumulative absorption.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of the test substance was adequately reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (1000 uL/cm2) and volume (64 uL) were delivered consistently across study groups to exposed skin. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered to be minor and unlikely to have an impact on the study results.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and appropriate for Kp determination. A steady state flux was obtained.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 3 dose groups tested in a wide range of concentrations (neat, 50%, and 10%). Dilutions of the test substance were performed in two different vehicles (isopropyl myristate or kerosene). The authors provided justification for the application rate (1000 uL/cm2), chosen to establish a non-depletable dose, and doses, as realistic operator exposures.
Domain 4: Test Model				

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 50% in kerosene

Domain	Metric		Rating	Comments
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. Measurement techniques and timing were reported and appropriate. An infinite dose of the test substance was used to determine the Kp. An application rate of 1000 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2.
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assess consistently across study replicates. The same duration of exposure, receptor fluid used, and sampling period was consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of >17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 50% in kerosene

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported for the cumulative amount of test substance in the receptor fluid at each time point. Mathematical calculations used to determine Kp were reported. The Kp was correctly based on the linear data phase of the absorption curve. CV values were not reported for Kp and could not be determined.
	Metric 20:	Data interpretation	High	The Kp values were derived from an appropriate exposure condition (infinite dose). Recovery was not reported but this determination is not relevant for infinite dose applications. Kps were calculated from the linear portion of the absorption curve.
	Metric 21:	Reporting of data	Medium	Data for cumulative absorption for each time point and cell were reported. Data were also reported as means ± SD. Calculated Kp were not reported with SD or CV.

Overall Quality Determination High

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 10% in kerosene

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,2-dichloropropane and radiolabeled [14C]-1,2-dichloropropane CAS number: 78-87-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The radiolabeled 1,2-dichloropropane was sourced from Moravek Inc. The non-radiolabeled, 1,2-dichloropropane was obtained from the sponsor (American Chemicals Council). The study included certificates of analyses that included lot/batch numbers and purity.
	Metric 3:	Test substance purity	High	The radiochemical purity of the radiolabeled test substance was reported to be 100% by HPLC. The purity of the non-radiolabeled substance was 99.9% by GCMS. Radiochemical purities of the prepared solution were determined by study authors using HPLC prior to application; all were ≥92.5%, and impurities were reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Caffeine (non-labelled and radiolabeled) were used as a reference compound. Data are fully reported for caffeine studies. 3.66 mg/ml was administered to the skin (5.7 mg/cm2); n=8. Study authors report the mean mass balance of 96.80% (CV = 3.14%), total absorbed dose (receptor fluids and receptor camber) 13.51% (CV=17%), and permeability coefficient (Kp) was 0.000195 cm/hr.
	Metric 5:	Assay procedures	High	This study was conducted according to OECD TG 428, and OECD 28. The assay procedures specified in the report were described in detail, although some information was missing. The static diffusion set-up is sufficiently reported including a photograph. The skin was placed into the chamber and allowed to equilibrate for a minimum of 30 minutes. The skin membranes were maintained at 32 +/-1 degree C; humidity was not reported but was monitored. Infinite doses of 1,2-dichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or kerosene) were applied to human skin (at least 8 replicates; surface area of 0.64 cm2). The volume applied (640 uL) was necessary to achieve the desired application rate of 1000 uL/cm2. Full-thickness abdominal human skin samples (from females ages 41-60 years) were obtained frozen from Tissue Solutions or BioIVT. The skin was allowed to thaw and dermatomed (thickness ranged from 360 to 400 um). The skin was exposed to the test substance under occluded conditions (carbon filter and pouch of Anasorb 747) for 24 hours. The receptor solution (phosphate-buffered saline fortified with 6% polyethoxyoleate 20 oleyl ether and gentamicin) was appropriate for this lipophilic chemical. The solubility of 1,2-dichloropropane was tested in the receptor fluid prior to the study and determined dissolution of 1,2-dichloropropane was not rate-limiting. The receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (300uL) were collected at 10 minutes, 30 minutes, 1, 2, 4, 8, 12, 16, 20, and 24 hours post-application and analyzed for radioactivity. An equal volume was replaced. Radioactivity was measured using a liquid scintillation counter with a blank sample subtracted from sample counts. “A limit of reliable measurement of 30 d.p.m. above background has been instituted in these laboratories”. A steady state was reached.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 10% in kerosene

Domain	Metric		Rating	Comments
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by electrical resistance and stable transepidermal water loss (TEWL) prior to dose application and at the end of the experiment. Any sample with a resistance of less than 7.7 kilo-ohms was excluded; this is lower than the recommended 17 kilo-ohms. TEWL readings were reported for both time 0 and 24 hours in Appendix 10, the majority of cells had readings of <10 grams/m2/hour at time 0. The percentage of the recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. The study did report a cumulative absorption in the receptor fluid at each time point. Coefficients of variation (CV) values were not reported for Kp, but could be calculated for cumulative absorption.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of the test substance was adequately reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution were reported; dilutions were vortexed. Homogeneity was assessed and dilutions were assessed by liquid scintillation counting. Results were reported. Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made or how they were stored. The solubility of the test substance in the receptor fluid was determined and was not rate-limiting.
	Metric 8:	Consistency of exposure administration	Medium	The application rate (1000 uL/cm2) and volume (64 uL) were delivered consistently across study groups to exposed skin. The skin surface area of 0.64 cm2 was consistent across groups. The skin thickness ranged from 360 to 400 uM which is considered to be minor and unlikely to have an impact on the study results.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as ug equiv./cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and appropriate for Kp determination. A steady state flux was obtained.
	Metric 11:	Number of exposure groups and concentration spacing	High	There were 3 dose groups tested in a wide range of concentrations (neat, 50%, and 10%). Dilutions of the test substance were performed in two different vehicles (isopropyl myristate or kerosene). The authors provided justification for the application rate (1000 uL/cm2), chosen to establish a non-depletable dose, and doses, as realistic operator exposures.
Domain 4: Test Model				

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 10% in kerosene

Domain	Metric		Rating	Comments
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness abdominal skin samples were obtained from 8 female donors (aged 41-60 years; race not reported). The samples arrived at the test laboratory deeply frozen on dry ice and were then stored frozen at -20 degrees C until use. The skin samples were thawed, and dermatomed using an electric dermatome. The thickness of the samples ranged from 360 to 400 uM. Membranes were then wrapped in foil, placed in a self-sealing bag and re-frozen, stored at -20 degrees C, for a maximum of 2 months. Membrane integrity was determined by measuring transepidermal water loss prior to/and upon completion of the experiment.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates was appropriate as per OECD 428. Guidelines recommend a minimum of 4 replicated per test preparation. This study examined 8 replicates/dose (from 4 donors).
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The outcome assessment methodology addressed the intended outcome of interest and was sensitive for the outcome. The test followed OECD guidelines 428 and 28. Measurement techniques and timing were reported and appropriate. An infinite dose of the test substance was used to determine the Kp. An application rate of 1000 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2.
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment protocol were reported and outcomes were assess consistently across study replicates. The same duration of exposure, receptor fluid used, and sampling period was consistent across replicates.
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcomes of interest; measurement sensitivity was sufficient. The sampling intervals were adequate. Methods for the determination of radioactivity are reported. Blank samples were subtracted from sample counts. A limit of reliable measurement of 30 d.p.m. above background was instituted by this laboratory. The limit of reliable measurements for each matrix in each test preparation is shown in Appendix 12. Individual scintillation counts were not shown. A graphical representation of absorption over time is shown.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study used a single batch of radiolabeled 1,2-chloropropane. Human abdominal skin was obtained from 8 female donors, ranging in age from 41 to 60 years old. The large age range may influence results. The split-thickness ranged from 360-400 um. Skin integrity was confirmed by measuring electrical resistance, and TEWL both pre and post-exposure. Only skin meeting the inclusion criteria of resistance ($\leq$ 7.7 kino-ohms) was included in the analysis. This is lower than the recommendation of >17 kilo-ohms but may be acceptable depending on the system used. All TEWL measurements are reported. The majority of the TEWL measurements at time 0 and 24 hours were $\leq$10 grams/m2/hour (recommended), however, there are several that were greater than 10 grams/m2/h.

Continued on next page . . .

. . . continued from previous page

Study Citation: Charles River Laboratories, (2024). The in vitro percutaneous absorption of radiolabelled 1,2-dichloropropane (PDC) in thirteen dose scenarios through human split-thickness skin.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 11831402; Linked HERO ID(s): 11831402, 11831403
Unique ID: Infinite; 10% in kerosene

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure; the test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported for the cumulative amount of test substance in the receptor fluid at each time point. Mathematical calculations used to determine Kp were reported. The Kp was correctly based on the linear data phase of the absorption curve. CV values were not reported for Kp and could not be determined.
	Metric 20:	Data interpretation	High	The Kp values were derived from an appropriate exposure condition (infinite dose). Recovery was not reported but this determination is not relevant for infinite dose applications. Kps were calculated from the linear portion of the absorption curve.
	Metric 21:	Reporting of data	Medium	Data for cumulative absorption for each time point and cell were reported. Data were also reported as means ± SD. Calculated Kp were not reported with SD or CV.

Overall Quality Determination — High

Study Citation:	DuPont, (2005). Propylene dichloride: In vitro dermal absorption rate testing.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	7461856
Unique ID:	1,2-DCP - Infinite exposure scenario

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The name and CASRN were provided. The chemical was positively identified. Physical and chemical properties were reported, and a structure with the position of the radiolabel was included.
	Metric 2:	Test substance source	High	The sources and lots of the labeled and unlabeled chemical was given. Certificates of Analysis were provided in an appendix.
	Metric 3:	Test substance purity	High	The purity was high (99.9% for the radiolabel purity and 99% for the unlabeled chemical). Purities of stock solutions were analytically verified; impurities were not listed, but could be identified from the provided radiograms
Domain 2: Test Design				
	Metric 4:	Reference compounds	Low	There was no reference compound identified. The experiments were conducted by E.I. du Pont de Nemours and Company. EPA could locate no information on past history of performing dermal absorption studies at this laboratory.
	Metric 5:	Assay procedures	Medium	The study was conducted according to OECD TG 428 and methods were described in detail. The study used epidermal membranes (40 to 64 µm) originating from human cadaver abdominal skin which is acceptable, although split thickness skin is preferred. The dose volume was 1200 uL/cm2, which is appropriate for an infinite exposure scenario. A static diffusion cell was used. The text did not specify whether constant stirring occurred.
	Metric 6:	Standards for tests	Medium	Criteria were provided for acceptable skin integrity and the LOD for radiolabeled results was 2 x above background. No criteria were noted for CV% but information was provided on variability.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	High	The authors verified that the compound was stable. The authors tested for homogeneity and used analytical results to calculate specific activity.
	Metric 8:	Consistency of exposure administration	Medium	Within different protocol groups, exposures were consistent across replicates.
	Metric 9:	Reporting of concentrations	High	Specific activity, volume applied, and surface area were all provided to allow specificity in amounts applied to skin.
	Metric 10:	Exposure frequency	High	The duration for the infinite exposure scenario was appropriate. The last collection was made 8 hours post-application following steady-state determination.
	Metric 11:	Number of exposure groups and concentration spacing	Low	Although not clearly stated, the doses seem to be neat - so only one dose was used for infinite doses (1200 ul/cm2). OECD TGs recommend the use of 3 doses or more. Conditions of use were not discussed in the study.
Domain 4: Test Model				

Continued on next page . . .

. . . continued from previous page

Study Citation: DuPont, (2005). Propylene dichloride: In vitro dermal absorption rate testing.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 7461856
Unique ID: 1,2-DCP - Infinite exposure scenario

Domain	Metric		Rating	Comments
	Metric 12:	Test model (skin)	High	The study used human cadaver skin that was heat-treated at 60 degrees C to separate the dermis from the epidermis. The resulting epidermal membrane thickness ranged from 40 to 64µm. The samples were from three donors, and skin integrity results were reported.
	Metric 13:	Number/Replicates per group	Medium	The study used 6 replicates from 3 donors for a single test concentration.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Medium	Infinite dosing was used for Kp determinations. Only neat test substance was used, and no discussion on the conditions of use was provided. It is unclear whether this appropriately represents conditions of use. The study used 1200 uL/cm2, which was appropriate for an infinite scenario and a steady state was obtained.
	Metric 15:	Consistency of outcome assessment	High	The outcome assessment protocols were reported and were consistent across groups.
	Metric 16:	Sampling adequacy and sensitivity	High	The sample size and sampling intervals were appropriate. The study reported the number of scintillation counts, and the LOD was set at twice the background.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The exposure areas (0.64 cm2) were consistent across replicates. Electrical impedance of each sample was tested prior to application of the test substance. Membranes with an EI of $\geq$17 kohms were considered acceptable, which is consistent with OECD test guidelines. Skin samples were from 3 donors. Although the protocol specifies that donor age and sex should be recorded, this information was not reported. All samples were from the abdominal region.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Low	The pH of the receptor fluid was 3.8. The authors stated that this did not have an impact on the study results, but there were changes in skin integrity and results were variable.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	The kp was determined from 4 time points once steady state was reached, but the authors do not state which 4 time points were used. The CV for the Kp measurement is >50%, but data are available for EPA to calculate an alternate upper-end value. Any outliers were identified and excluded where appropriate
	Metric 20:	Data interpretation	Medium	Total recovery was 94.5%. Kp was determined from an infinite exposure scenario.
	Metric 21:	Reporting of data	High	Data were reported for all exposures and times taken.

Overall Quality Determination — Medium

Study Citation: DuPont, (2005). Propylene dichloride: In vitro dermal absorption rate testing.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 7461856
Unique ID: 1,2-DCP - finite exposure - 10 min duration

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The name and CASRN were provided. The chemical was positively identified. Physical and chemical properties were reported, and a structure with the position of the radiolabel was included.
	Metric 2:	Test substance source	High	The sources and lots of the labeled and unlabeled chemical was given. Certificates of Analysis were provided in an appendix.
	Metric 3:	Test substance purity	High	The purity was high (99.9% for the radiolabel purity and 99% for the unlabeled chemical). Purities of stock solutions were analytically verified; impurities were not listed, but could be identified from the provided radiograms
Domain 2: Test Design				
	Metric 4:	Reference compounds	Low	There was no reference compound identified. The experiments were conducted by E.I. du Pont de Nemours and Company. EPA could locate no information on past history of performing dermal absorption studies at this laboratory.
	Metric 5:	Assay procedures	Medium	The study was conducted according to OECD TG 428. The study used epidermal membranes (40 to 64 μm) originating from human cadaver abdominal skin which is acceptable, although split thickness skin is preferred. The dose volume was 20 uL/cm2, which is greater than the recommended maximum of 10 μL/cm2 for a finite study. A static diffusion cell was used. The text did not specify whether constant stirring occurred.
	Metric 6:	Standards for tests	Medium	Criteria were provided for acceptable skin integrity and the LOD for radiolabeled results was 2 x above background. No criteria were noted for CV% but information was provided on variability.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	High	The authors verified that the compound was stable. The authors tested for homogeneity and used analytical results to calculate specific activity.
	Metric 8:	Consistency of exposure administration	Medium	Within different protocol groups, exposures were consistent across replicates.
	Metric 9:	Reporting of concentrations	High	Specific activity, volume applied, and surface area were all provided to allow specificity in amounts applied to skin.
	Metric 10:	Exposure frequency	Low	Finite exposures were terminated at 10 min or at 60 minutes, and no collections were made beyond these time points. Generally, a sampling period of 24 hours is required to adequately characterize the absorption profile, although less time may be appropriate for substances that penetrate the skin rapidly. The authors provided no justification for the durations selected for the short-term exposure experiments.
	Metric 11:	Number of exposure groups and concentration spacing	Low	Although not clearly stated, the doses seem to be neat - so only one dose was used for infinite doses (1200 ul/cm2). OECD TGs recommend the use of 3 doses or more. Conditions of use were not discussed in the study.
Domain 4: Test Model				

Continued on next page . . .

. . . continued from previous page

Study Citation: DuPont, (2005). Propylene dichloride: In vitro dermal absorption rate testing.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 7461856
Unique ID: 1,2-DCP - finite exposure - 10 min duration

Domain	Metric		Rating	Comments
	Metric 12:	Test model (skin)	High	The study used human cadaver skin that was heat-treated at 60 degrees C to separate the dermis from the epidermis. The resulting epidermal membrane thickness ranged from 40 to 64µm. The samples were from three donors, and skin integrity results were reported.
	Metric 13:	Number/Replicates per group	Medium	The study included 6 replicates total per time point. Each termination time had data from 3 donors (2 replicates each)
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Medium	Finite dosing was used to determine short-term absorption rates; total absorbed amounts (based on measurements in RF and Skin) were reported as ug equivalents. The dose volume 20 uL/cm2 for a neat test substance is larger than specified in OECD TG 428. It is unclear whether neat exposures represent conditions of use.
	Metric 15:	Consistency of outcome assessment	High	The outcome assessment protocols were reported and were consistent across groups.
	Metric 16:	Sampling adequacy and sensitivity	Medium	The sample sizes were appropriate. However, no sampling was conducted after the exposure duration. The study reported the number of scintillation counts and the LOD was set at twice the background.et at twice the background.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The exposure areas (0.64 cm2) were consistent across replicates. Electrical impedance of each sample was tested prior to application of the test substance. Membranes with an EI of $\geq$17 kohms were considered acceptable, which is consistent with OECD test guidelines. Skin samples were from 3 donors. Although the protocol specifies that donor age and sex should be recorded, this information was not reported. All samples were from the abdominal region.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Low	The pH of the receptor fluid was 3.8. The authors stated that this did not have an impact on the study results, but there were changes in skin integrity and results were variable.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	For the finite scenarios, absorption percentages were not provided across time points.Any outliers were identified and excluded where appropriate. The CVs for total absorbed were 53% for the 10 min exposure and 49% for the 60 min, indicating large variability in the results. Data are available for EPA to calculate an alternate upper-end value.
	Metric 20:	Data interpretation	Low	Total recovery was 77.8% for the 10 min duration test. The study authors noted that OECD Guidelines specify a recovery of 100$\pm$10% is acceptable or 100 $\pm$ 20% for volatile compounds. In this study, large amounts of the test substance were detected in the vapor traps, suggesting high volatility. The authors did not report whether results were normalized. Tape stripping was not conducted and may not be appropriate for exposures on epidermal membranes. Total absorbed amounts and penetration rates were determined from finite exposure scenarios.
	Metric 21:	Reporting of data	High	Data were reported for all exposures and times taken.

Continued on next page . . .

. . . continued from previous page

Study Citation:	DuPont, (2005). Propylene dichloride: In vitro dermal absorption rate testing.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	7461856
Unique ID:	1,2-DCP - finite exposure - 10 min duration

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	

Study Citation: DuPont, (2005). Propylene dichloride: In vitro dermal absorption rate testing.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 7461856
Unique ID: 1,2-DCP - finite exposure - 60 min duration

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The name and CASRN were provided. The chemical was positively identified. Physical and chemical properties were reported, and a structure with the position of the radiolabel was included.
	Metric 2:	Test substance source	High	The sources and lots of the labeled and unlabeled chemical was given. Certificates of Analysis were provided in an appendix.
	Metric 3:	Test substance purity	High	The purity was high (99.9% for the radiolabel purity and 99% for the unlabeled chemical). Purities of stock solutions were analytically verified; impurities were not listed, but could be identified from the provided radiograms
Domain 2: Test Design				
	Metric 4:	Reference compounds	Low	There was no reference compound identified. The experiments were conducted by E.I. du Pont de Nemours and Company. EPA could locate no information on past history of performing dermal absorption studies at this laboratory.
	Metric 5:	Assay procedures	Medium	The study was conducted according to OECD TG 428. The study used epidermal membranes (40 to 64 μm) originating from human cadaver abdominal skin which is acceptable, although split thickness skin is preferred. The dose volume was 20 uL/cm2, which is greater than the recommended maximum of 10 μL/cm2 for a finite study. A static diffusion cell was used. The text did not specify whether constant stirring occurred.
	Metric 6:	Standards for tests	Medium	Criteria were provided for acceptable skin integrity and the LOD for radiolabeled results was 2 x above background. No criteria were noted for CV% but information was provided on variability.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	High	The authors verified that the compound was stable. The authors tested for homogeneity and used analytical results to calculate specific activity.
	Metric 8:	Consistency of exposure administration	Medium	Within different protocol groups, exposures were consistent across replicates.
	Metric 9:	Reporting of concentrations	High	Specific activity, volume applied, and surface area were all provided to allow specificity in amounts applied to skin.
	Metric 10:	Exposure frequency	Low	Finite exposures were terminated at 10 min or at 60 minutes, and no collections were made beyond these time points. Generally, a sampling period of 24 hours is required to adequately characterize the absorption profile, although less time may be appropriate for substances that penetrate the skin rapidly. The authors provided no justification for the durations selected for the short-term exposure experiments.
	Metric 11:	Number of exposure groups and concentration spacing	Low	Although not clearly stated, the doses seem to be neat - so only one dose was used for infinite doses (1200 ul/cm2). OECD TGs recommend the use of 3 doses or more. Conditions of use were not discussed in the study.
Domain 4: Test Model				

Continued on next page . . .

. . . continued from previous page

Study Citation: DuPont, (2005). Propylene dichloride: In vitro dermal absorption rate testing.
Chemical: 1,2-Dichloropropane
Exposure Type: Parent compound
HERO ID: 7461856
Unique ID: 1,2-DCP - finite exposure - 60 min duration

Domain	Metric		Rating	Comments
	Metric 12:	Test model (skin)	High	The study used human cadaver skin that was heat-treated at 60 degrees C to separate the dermis from the epidermis. The resulting epidermal membrane thickness ranged from 40 to 64µm. The samples were from three donors, and skin integrity results were reported.
	Metric 13:	Number/Replicates per group	Medium	The study included 6 replicates total per time point. Each termination time had data from 3 donors (2 replicates each)
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Medium	Finite dosing was used to determine short-term absorption rates; total absorbed amounts (based on measurements in RF and Skin) were reported as ug equivalents. The dose volume 20 uL/cm2 for a neat test substance is larger than specified in OECD TG 428. It is unclear whether neat exposures represent conditions of use.
	Metric 15:	Consistency of outcome assessment	High	The outcome assessment protocols were reported and were consistent across groups.
	Metric 16:	Sampling adequacy and sensitivity	Medium	The sample sizes were appropriate. However, no sampling was conducted after the exposure duration. The study reported the number of scintillation counts and the LOD was set at twice the background.et at twice the background.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The exposure areas (0.64 cm2) were consistent across replicates. Electrical impedance of each sample was tested prior to application of the test substance. Membranes with an EI of $\geq$17 kohms were considered acceptable, which is consistent with OECD test guidelines. Skin samples were from 3 donors. Although the protocol specifies that donor age and sex should be recorded, this information was not reported. All samples were from the abdominal region.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Low	The pH of the receptor fluid was 3.8. The authors stated that this did not have an impact on the study results, but there were changes in skin integrity and results were variable.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	For the finite scenarios, absorption percentages were not provided across time points.Any outliers were identified and excluded where appropriate. The CVs for total absorbed were 53% for the 10 min exposure and 49% for the 60 min, indicating large variability in the results. Data are available for EPA to calculate an alternate upper-end value.
	Metric 20:	Data interpretation	Medium	Total recovery was 87.8% for the 60 min duration test. The study authors noted that OECD Guidelines specify a recovery of 100$\pm$10% is acceptable or 100 $\pm$ 20% for volatile compounds. In this study, large amounts of the test substance were detected in the vapor traps, suggesting high volatility. The authors did not report whether results were normalized. Tape stripping was not conducted and may not be appropriate for exposures on epidermal membranes. Total absorbed amounts and penetration rates were determined from finite exposure scenarios.
	Metric 21:	Reporting of data	High	Data were reported for all exposures and times taken.

Continued on next page . . .

. . . continued from previous page

Study Citation:	DuPont, (2005). Propylene dichloride: In vitro dermal absorption rate testing.
Chemical:	1,2-Dichloropropane
Exposure Type:	Parent compound
HERO ID:	7461856
Unique ID:	1,2-DCP - finite exposure - 60 min duration

Domain	Metric	Rating	Comments
Overall Quality Determination		**Medium**	